American Heart Journal

VOL. 44 NOVEMBER, 1952 NO. 5

Original Communications

A BALLISTOCARDIOGRAPHIC AND ELECTROCARDIOGRAPHIC STUDY OF 328 PATIENTS WITH CORONARY ARTERY DISEASE: COMPARISON WITH RESULTS FROM A SIMILAR STUDY OF APPARENTLY NORMAL PERSONS

W. R. SCARBOROUGH, M.D.,* R. E. MASON, M.D., F. W. DAVIS, JR., M.D.,**
M. L. SINGEWALD, M.D., B. M. BAKER, JR., M.D., AND S. A. LORE

BALTIMORE, MD.

THE CHARACTERISTICS of the symptom complex termed "angina pectoris" have been known for 180 years[1] and have been fully and frequently described. It has long been recognized that angina pectoris is one of the clinical manifestations of coronary artery disease. In its classical form angina pectoris is not difficult to recognize but there are numerous variants which do not fit the classical pattern and lead to confusion regarding diagnosis. Because of these perplexing types of "atypical chest pain" and because one is loath to base a diagnosis of such importance entirely upon subjective symptoms, clinicians and investigators have for many years sought a method which could supply objective evidence for the existence of coronary artery disease. The electrocardiograph has become a valuable and almost indispensable aid in the diagnosis of acute myocardial infarction but it is of limited value in those forms of coronary artery disease in which there has been no necrosis or ischemia of large areas of heart muscle. Inasmuch as inadequacy of blood supply to the heart muscle is more apparent under conditions which demand increased work from the heart, most of the recent diagnostic methods depend on changes in the electrocardiogram during or following stress-producing procedures. These methods have contributed much to the diagnosis of coronary artery disease but they still leave much to be desired.

From the Department of Medicine, Johns Hopkins University School of Medicine and Hospital, Baltimore, Md.

Supported by a Research Grant from the National Heart Institute of the National Institutes of Health, United States Public Health Service.

Received for publication April 18, 1952.

*Read Ellsworth Fellow in Medicine.

**Post-Doctorate Fellow, National Heart Institute.

TABLE I. 137 PATIENTS WITH OLD MYOCARDIAL INFARCTION

SEX OF PATIENTS	*	AGE: 30-39 YEARS				AGE: 40-49 YEARS				AGE: 50-59 YEARS				AGE: 60-69 YEARS				AGE: 70-79 YEARS				TOTALS			
		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Men	N	6	42.8	1	7.1	11	28.9	8	21.0	3	6.5	7	15.2	0	0	3	13.6					20	16.7	19	15.8
	B	3	21.5	1	7.1	5	13.2	5	13.2	6	13.1	3	6.5	1	4.6	4	18.2					15	12.5	13	10.8
	A	5	35.7	12	85.8	22	57.9	25	65.8	37	80.4	36	78.3	21	95.4	15	68.2					85	70.8	88	73.4
Women	N	1	50	1	50	1	25	2	50	0	0	1	14.2	0	0	1	33.3	0	0	0	0	2	11.8	5	29.4
	B	0	0	0	0	0	0	1	25	1	14.3	3	42.9	0	0	2	66.7	0	0	0	0	1	5.9	6	35.3
	A	1	50	1	50	3	75	1	25	6	85.7	3	42.9	3	100	0	0	1	100	1	100	14	82.3	6	35.3
Combined (Men and Women)	N	7	43.7	2	12.6	12	28.6	10	23.8	3	5.7	8	15.1	0	0	4	16.0	0	0	0	0	22	16.1	24	17.4
	B	3	18.8	1	6.2	5	11.9	6	14.3	7	13.2	6	11.3	1	4.0	6	24.0	0	0	0	0	16	11.2	19	14.0
	A	6	37.5	13	81.2	25	59.5	26	61.9	43	81.1	39	73.6	24	96.0	15	60.0	1	100	1	100	99	72.2	94	68.6
Total Cases	Men	14				38				46				22								120			
	Women	2				4				7				3				1				17			
	Combined	16				42				53				25				1				137			

*N = normal, B = borderline, and A = abnormal.

Starr's[2] development of the ballistocardiograph has recently made possible a new approach to the diagnosis of coronary artery disease. He has shown that the size and shape of the ballistocardiographic pattern is dependent upon the manner in which the heart ejects its blood. Hearts which contract with great force and vigor produce large complexes with a characteristic wave form. When cardiac contraction is weak, regardless of its cause, the complexes are small and/or abnormal in form. Patients with coronary artery disease frequently show abnormal ballistocardiograms and therefore evidence of decrease in the strength of cardiac contraction; thus, in patients without signs of other types of heart disease, abnormal ballistocardiograms may supply indirect evidence for the existence of coronary artery disease. The fact that the ballistocardiogram often provides the only objective indication of cardiac disease is of considerable importance since physical examination, the chest roentgenogram, and the electrocardiogram may all be normal in such patients. The simplicity of the method is a great advantage, for all that is required of a patient is that he lie quietly on the ballistograph bed for a few minutes.

Recently, a number of reports have appeared in the literature regarding the application of the ballistocardiograph to the study of patients with coronary artery disease (see Discussion). In these studies use was made of the Starr high-frequency bed, the Nickerson low-frequency bed and the direct-body pickups (electromagnetic and photoelectric) introduced by Dock. All are in general agreement with respect to the high incidence of abnormal ballistocardiograms in patients with coronary artery disease.

In a previous report[3] the electrocardiographic and ballistocardiographic findings in a group of 110 patients with coronary artery disease were presented. A high percentage of these patients had abnormal ballistocardiograms but there was no normal series to which these findings could be referred for comparison. Since then a large number of normal persons of all ages have been studied and their findings have been summarized in a companion report.[4] In addition, the number of patients with coronary artery disease studied has been very considerably increased. The purpose of the present communication is to report the electrocardiographic and ballistocardiographic findings in 191 cases of angina pectoris and 137 cases of old myocardial infarction and to compare them with the findings in 369 individuals with no symptoms or signs of cardiovascular disease.

MATERIALS AND METHODS

Three hundred twenty-eight patients with coronary artery disease were studied. There were 137 with a history of old myocardial infarction. None of these patients was studied until at least six weeks had elapsed after the acute attack. Their ages ranged from 31 to 79 years. There were 120 men and 17 women. The age and sex distributions are shown in Table I.

There were 191 patients with angina pectoris. The diagnosis in this group was based entirely on a typical symptomatic history. Patients with angina pectoris known to have had myocardial infarctions were placed in the myocardial infarction group only. Ages ranged from 34 to 81 years. There were 151 men and 40 women. The age and sex distributions are shown in Table II.

TABLE II. 191 PATIENTS WITH ANGINA PECTORIS

SEX OF PATIENTS	*	AGE: 30-39 YEARS				AGE: 40-49 YEARS				AGE: 50-59 YEARS				AGE: 60-69 YEARS				AGE: 70-79 YEARS				AGE: 80-89 YEARS				TOTALS			
		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG		BCG		ECG	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Men	N	3	33.3	4	44.5	9	23.7	19	50.0	7	11.6	35	58.4	3	7.9	14	36.8	0	0	5	83.3					22	14.5	77	51.0
	B	2	22.2	2	22.2	11	28.9	11	28.9	6	10.0	13	21.6	2	5.3	10	26.4	0	0	0	0					21	13.9	36	23.8
	A	4	44.5	3	33.3	18	47.4	8	21.1	47	78.4	12	20.0	33	86.8	14	36.8	6	100	1	16.7					108	71.6	38	25.2
Women	N					0	0	7	70.0	0	0	10	58.8	0	0	2	22.2	0	0	1	33.3	0	0	1	100	0	0	21	52.5
	B					1	10.0	2	20.0	3	17.6	6	35.3	0	0	3	33.3	0	0	0	0	0	0	0	10	4	10	11	27.5
	A					9	90.0	1	10.0	14	82.4	1	5.9	9	100	4	44.5	3	100	2	66.7	1	100	0	0	36	90.0	8	20.0
Combined (Men and Women)	N	3	33.3	4	44.5	9	18.8	26	54.2	7	9.1	45	58.5	3	6.4	16	34.1	0	0	6	66.7	0	0	1	100	22	11.5	98	51.3
	B	2	22.2	2	22.2	12	25.0	13	27.1	9	11.7	19	24.7	2	4.3	13	27.7	0	0	0	0	0	0	0	0	25	13.1	47	24.6
	A	4	44.5	3	33.3	27	56.2	9	18.7	61	79.2	13	16.8	42	89.3	18	38.2	9	100	3	33.3	1	100	0	0	144	75.4	46	24.1
Total Cases		Men 9				38				60				38				6				0				151			
		Women 0				10				17				9				3				1				40			
		Combined 9				48				77				47				9				1				191			

*N = normal, B = borderline, and A = abnormal.

All patients who had conditions other than coronary artery disease likely to produce electrocardiographic or ballistocardiographic abnormalities were excluded from the study. However, patients with both coronary artery disease and hypertension were admitted inasmuch as an earlier study revealed that there was no significant difference between normotensive and hypertensive angina pectoris patients with respect to ballistocardiographic abnormality.

The age distribution curves for both the angina pectoris and old myocardial infarction groups show a somewhat larger number of young patients with coronary artery disease than would be obtained in unselected samples. This is a result of efforts made to secure as many young patients as possible for study. Among the patients with myocardial infarction are eight who were included in a report by Yater and associates[5] on coronary artery disease occurring in young men in the military service.

All patients had complete electrocardiographic surveys which included the standard and unipolar limb leads and six unipolar precordial leads. All electrocardiograms were read by one of us and were classified as normal, borderline, or abnormal on the basis of generally accepted criteria. All patients had complete ballistocardiographic surveys recorded on a high-frequency bed; these included the conventional head-foot record as well as ballistocardiographic "vector" records taken by means of a technique previously described.[6] In most of the subjects ballistocardiograms were taken before and during abdominal compression produced by inflating a blood pressure cuff to 30 mm. Hg pressure beneath a snug abdominal binder. The Master "two-step" exercise test was performed on some of the patients; electrocardiograms and in some cases ballistocardiograms were recorded immediately and at intervals after the termination of exercise. The Master[7] criteria were used to evaluate the electrocardiographic changes produced by exercise. All control ballistocardiograms were read by one of us and were qualitatively classified as normal, borderline, or abnormal on the basis of wave form in the conventional head-foot record.

The ballistocardiograms classified as normal and borderline were treated in a manner similar to those so classified in a large group of apparently normal subjects; some sixty variables were measured from the records and were analyzed statistically. The measurements from these normal and borderline records from the coronary artery disease group were compared with those in the same categories from the normal control group and significant differences were sought. The composition and characteristics of the clinically normal group have been delineated elsewhere.[4]

RESULTS

A. Old Myocardial Infarction Group.—

1. *General*: Table I shows the electrocardiographic and ballistocardiographic findings by sex and age group in the 137 patients with old myocardial infarction. Fig. 1 shows the frequency of abnormal electrocardiograms and ballistocardiograms in each age group for the combined men and women. The black arrowheads indicate the frequency of abnormal records in a large group of normal persons reported elsewhere.[4]

As expected, the frequency of abnormal electrocardiograms was high when old myocardial infarction was present, regardless of the age of the patient. Electrocardiograms were abnormal in 68.6 per cent of the 137 cases. On the other hand the frequency of ballistocardiographic abnormality showed a distinct age trend; only 38 per cent of the records in the fourth decade were abnormal but the incidence rose to 96 per cent in the seventh decade. There were significant differences in incidence of ballistic abnormality from one decade to the next in all but the third to fourth decades. The increase in frequency of abnormal ballisto-

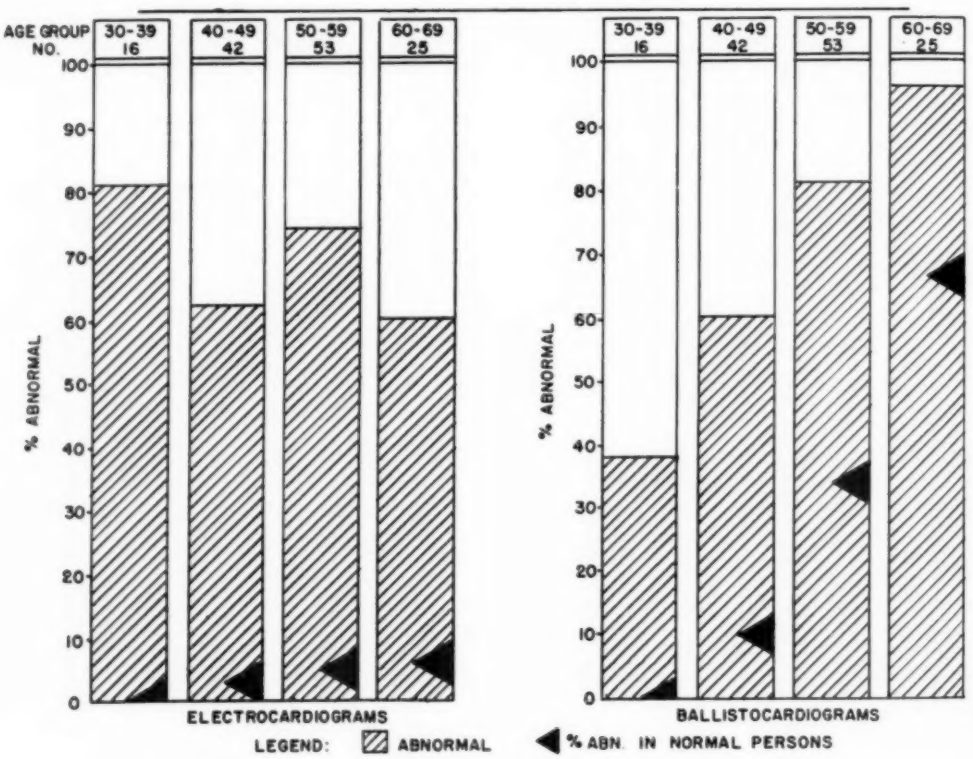


Fig. 1.—Electrocardiographic and ballistocardiographic study of 137 cases of old myocardial infarction. Number of patients in each decade is indicated below the age group designation. Electrocardiograms abnormal in 69 per cent and ballistocardiograms abnormal in 72 per cent of whole group; both incidences are significantly higher than in clinically normal persons (arrowheads). There is an increasing frequency of ballistocardiographic form abnormality with age in patients with myocardial infarction as well as in normal subjects. Only 38 per cent of the patients below the age of 40 had abnormal ballistocardiograms but the incidence increased to 96 per cent in the seventh decade.

cardiograms with age in this group is quite similar to that in the normal group, but in each decade the percentage of abnormal records is significantly higher in the patients with old infarction than in the normal subjects. The incidence of abnormal ballistocardiograms in the whole group of 137 patients with old myocardial infarction was 72.2 per cent, a figure comparable to that for abnormal electrocardiograms. In only four patients (2.9 per cent) were both ballistocardiograms and electrocardiograms normal, whereas in sixty-eight (49.6 per cent) both records were abnormal. There were 125 patients (91.2 per cent) who

had either an abnormal ballistocardiogram, an abnormal electrocardiogram, or both. Table IIIA shows the relationship between the electrocardiographic and ballistocardiographic findings.

TABLE IIIA. OLD MYOCARDIAL INFARCTION

		BCG							
	*	N		B		A		TOTALS	
		NO.	%	NO.	%	NO.	%	NO.	%
ECG	N	4	(2.9)†	3	(2.2)	17	(12.4)	24	(17.5)
	B	3	(2.2)	2	(1.5)	14	(10.2)	19	(13.9)
	A	15	(11.0)	11	(8.0)	68	(49.6)	94	(68.6)
Totals		22	(16.1)	16	(11.7)	99	(72.2)	137	(100.0)

*N = normal, B = borderline, and *A* = abnormal.
†Per cent figure in parenthesis refers to the percentage of the whole group falling into a given block.

It is of interest that the incidence of abnormal ballistocardiograms was higher in women than in men in each age decade. This was also true of the group as a whole but the difference (11.5 per cent) was not statistically significant.

2. *Ballistocardiographic findings on young myocardial infarction patients*: The patients under the age of 40 years deserve special attention. There were sixteen subjects in this group, fourteen men and two women. They were all in their thirties at the time the studies were made, the average age being 37. In four, less than one year had elapsed since the acute infarction but in five the infarction had occurred seven years or more before. In five patients infarction had occurred before the age of 30 (two at 28, and three at 29 years). Precise information regarding the presence or absence of symptoms following infarction was available in ten. Nine of these were having attacks of angina pectoris and the ballistocardiogram was normal in four, abnormal in three, and borderline in two. Although there was no close correlation, those with severe symptoms generally had abnormal records and those with mild symptoms had normal ones. One patient, two years after his infarction, was asymptomatic, his electrocardiogram had returned to normal, and his ballistocardiogram was normal. In contrast, another patient had two infarctions, the first ten years before at the age of 28. Since then he has had severe angina pectoris and at the time his studies were made he was found to be in mild cardiac failure with gallop rhythm. His grossly abnormal ballistocardiograms, shown in Fig. 2, reveal large diastolic waves which tend to dominate the records. However, the majority of the young patients (62 per cent of those below 40) had normal or borderline records. The ballistocardiograms from one of these are shown in Fig. 3,*A*. The head-foot record is normal but shows rather short expiratory K waves. Abdominal compression improves ballistic form, increases amplitude, and practically eliminates respiratory variation. Fig. 4 contrasts the normal head-foot records from a normal 81-year-old man and a 36-year-old patient with myocardial infarction with the abnormal record from a 45-year-old patient with infarction.

3. *Summary*: In a group of 137 patients with old myocardial infarction the ballistocardiogram was abnormal in 72 per cent and the electrocardiogram was abnormal in 69 per cent; one or both were abnormal in 91 per cent. There was no age trend for electrocardiographic abnormality but there was for the

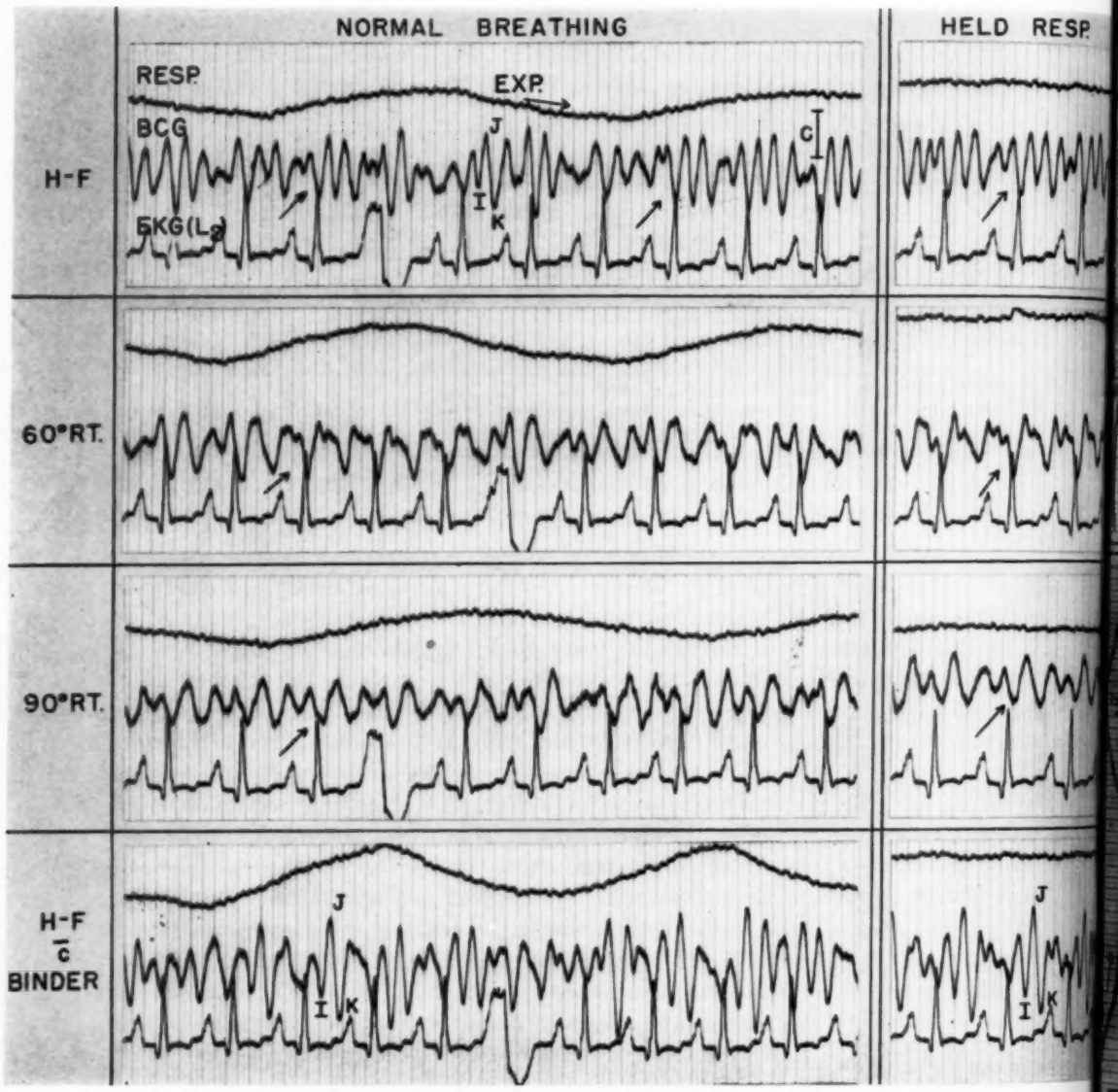


Fig. 2.—C. S., a 38-year-old man with history of two myocardial infarctions, first at age of 28. He has angina pectoris, mild congestive failure with presystolic gallop, cardiac enlargement, and blood pressure of 140/112 mm. Hg. The head-foot (H-F) ballistocardiogram is distinctly abnormal and shows large presystolic deflections which ride into and distort the systolic complexes. These are more clearly seen in the 60° Rt. and 90° Rt. (lateral) vector records; note the deep downward deflection which is synchronous with the QRS complex. Abdominal binder increases amplitude, improves form, and reduces size of oscillations arising in presystole; normal complexes are now present during held respiration. The bracketed vertical line marked *C* on these and all other records represents the calibration (1 cm. = 280 Gm.).

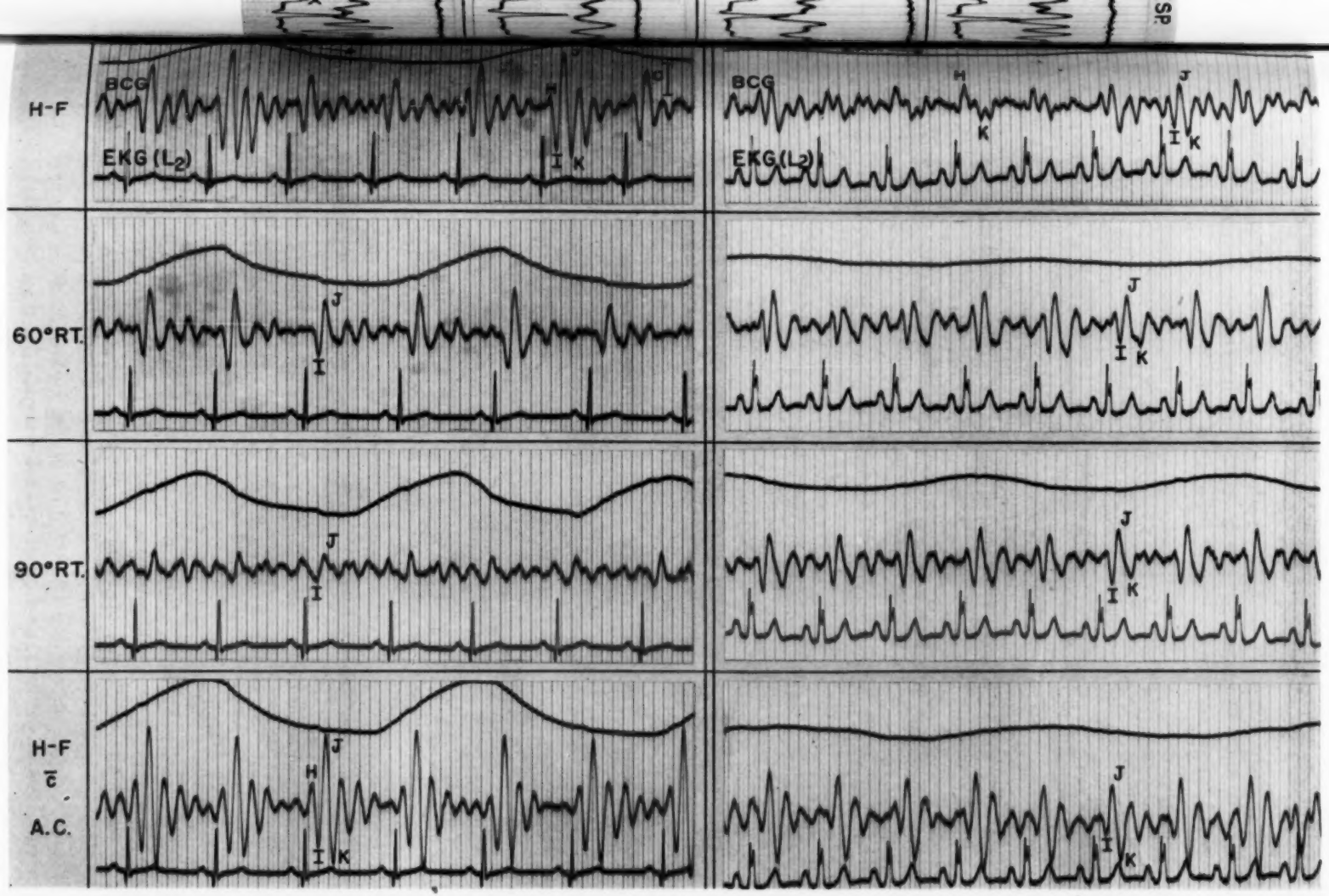


Fig. 3.—*A*, A. H., a 46-year-old man with old myocardial infarction. Head-foot (H-F) record is normal but there are rather short expiratory K waves and considerable respiratory variation in amplitude. Vector records (60° Rt., 90° Rt.) show pattern usually associated with normal head-foot record. 30 mm. Hg abdominal compression (A. C.) improves form, increases amplitude, and reduces respiratory variation (lower record).

B, R. P., a 59-year-old patient with diabetes and angina pectoris. The majority of the complexes in the head-foot ballistocardiogram are abnormal but those in the 60° Rt. and 90° Rt. vector records are tall and "normal" in form. Abdominal compression (30 mm. Hg) produces striking improvement in the head-foot record. Although the I waves are short and the K waves deep, all complexes are generally normal in form, amplitude is increased, and respiratory variation is reduced.

frequency of ballistocardiographic abnormality. Only 54 per cent of the ballistocardiograms from patients below the age of 50 were abnormal whereas 86 per cent of those above 50 were abnormal. The frequency of abnormal ballistocardiograms and electrocardiograms was significantly higher in patients with myocardial infarction than in normal subjects of comparable ages.

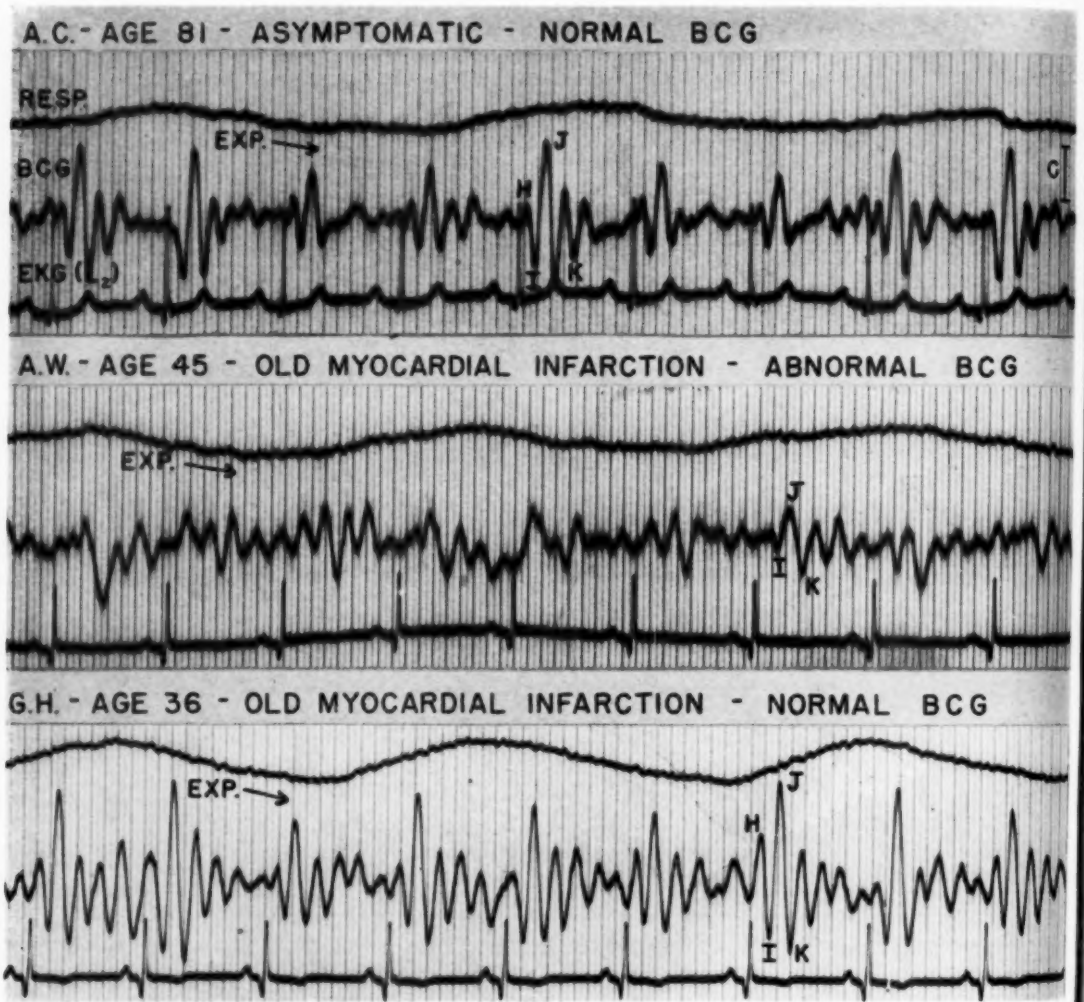


Fig. 4.—A comparison of the normal ballistocardiograms from an aged normal man and a 36-year-old patient with infarction with the abnormal ballistocardiogram from a 45-year-old patient with infarction. Normal ballistocardiograms in young patients with coronary artery disease are not uncommon, but they are uncommon in elderly normal persons.

B. Angina Pectoris Group.—

1. *General*: Table II shows the electrocardiographic and ballistocardiographic findings by sex and age group in the 191 patients with angina pectoris. Fig. 5 shows the frequency of abnormal electrocardiograms and ballistocardiograms in each age decade group for the combined men and women. There were only nine patients in the fourth and nine in the eighth decades but relatively large numbers in the fifth, sixth, and seventh decades.

In the patients with angina pectoris, unlike those with myocardial infarction, there was a low incidence of electrocardiographic abnormality. Only 24.1 per cent of the whole group had abnormal records. However, the differences between normal subjects and patients with angina pectoris were statistically significant in all decades except the eighth. There was no apparent age trend in the patients with angina pectoris.

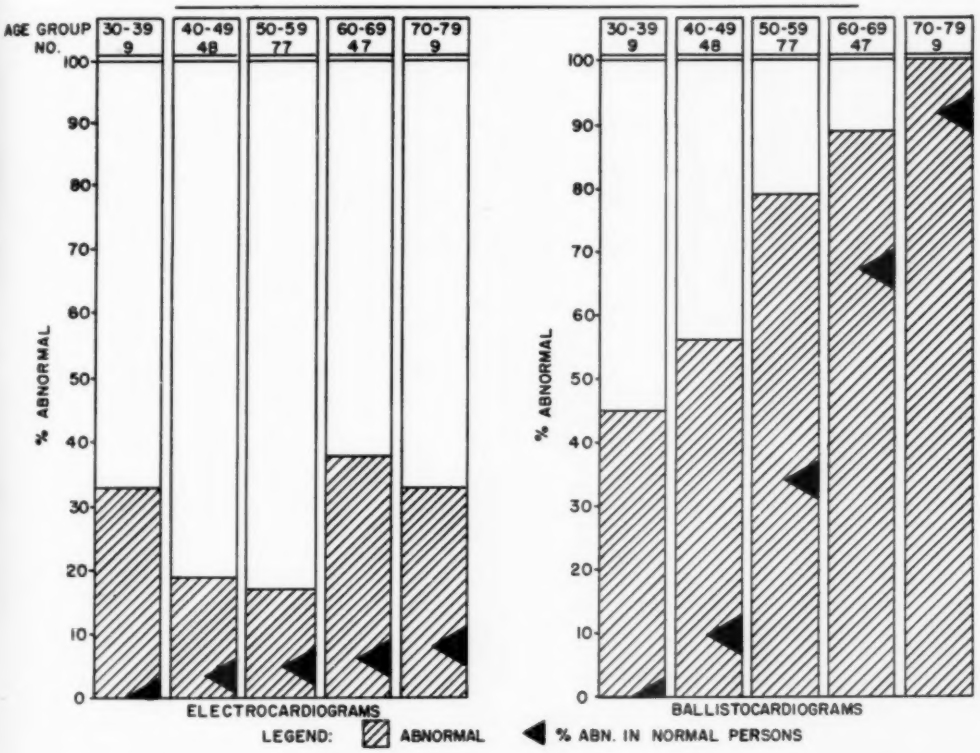


Fig. 5.—Electrocardiographic and ballistocardiographic study of 191 cases of angina pectoris. There is a low incidence of electrocardiographic abnormality (24 per cent, for the whole group) and a high incidence of ballistocardiographic abnormality (75 per cent, for the whole group). The frequency of abnormal electrocardiograms and ballistocardiograms is significantly higher in the patients with angina pectoris than in the normal control subjects (arrowheads) in each decade except the eighth. There is an increasing frequency of abnormal ballistocardiograms in patients as well as in normal subjects. Only 45 per cent of the patients in the fourth decade had abnormal ballistocardiograms; this incidence rose to 100 per cent in the eighth decade.

In contrast, there was a high incidence of ballistocardiographic abnormality and there was the same age trend that was noted in the patients with old myocardial infarction. Only 44.5 per cent of the patients in the fourth decade had abnormal ballistocardiograms but there was a progressive rise with age, reaching a peak of 100 per cent in the eighth decade. Considering the group as a whole, 75.4 per cent of the patients had abnormal records. Of apparently normal persons, 30.6 per cent over the same age range had abnormal ballistocardiograms. The difference between the two percentages is highly significant.

In seventeen patients (8.9 per cent) both electrocardiogram and ballistocardiogram were normal; in forty-three (22.5 per cent) both were abnormal (Table IIIB). In one hundred forty-eight (77.5 per cent), either the ballisto-

cardiogram, the electrocardiogram, or both were abnormal. This is only slightly higher than the frequency of abnormal ballistocardiograms alone. Only one of the twenty-two patients with normal ballistocardiograms had an abnormal electrocardiogram. The percentage of abnormal ballistocardiograms was significantly higher than that of abnormal electrocardiograms in all decades except the fourth.

TABLE IIIB. ANGINA PECTORIS

		BCG							
	*	N		B		A		TOTALS	
		NO.	%	NO.	%	NO.	%	NO.	%
ECG	N	17	(8.9)†	15	(7.8)	66	(34.6)	98	(51.3)
	B	4	(2.1)	7	(3.6)	36	(18.9)	47	(24.6)
	A	1	(0.5)	2	(1.1)	43	(22.5)	46	(24.1)
Totals		22	(11.5)	24	(12.5)	145	(76.0)	191	(100.0)

*N = normal, B = borderline, and A = abnormal.
†Per cent figure in parenthesis refers to the percentage of the whole group falling into a given block.

Like the women with myocardial infarction, those with angina pectoris had an incidence of abnormal ballistocardiograms which was equal to or higher than that in men in all age decades. Among the forty women, 90 per cent had abnormal records; this is 18 per cent higher than, and significantly different from, the corresponding percentage in men. In contrast, among normal subjects abnormal records were as frequent in men as in women.

2. *Exercise tests*: Single "two-step" exercise (Master) tests were performed on forty of the patients with angina pectoris with normal or borderline resting electrocardiograms. Out of this forty, seventeen (42.5 per cent) were positive tests. If it be assumed that the 145 patients with normal or borderline electrocardiograms would yield about the same proportion of positive Master tests as did the smaller group of forty, then one can determine the percentage of the entire group of 191 patients who would have either an abnormal resting electrocardiogram or a positive Master test. This percentage is 56.6. Master tests therefore increased the electrocardiographic "abnormality" from 24.1 to 56.6 per cent, a figure which is, nevertheless, significantly smaller than that for the incidence of abnormality in the resting ballistocardiograms.

In ten patients with normal or borderline resting ballistocardiograms, records were taken after a single Master test. Six of these became abnormal, two were unchanged, and two showed equivocal changes. Three of these same ten patients had a positive electrocardiographic response to the test. The small number of cases did not allow a satisfactory correlation between electrocardiographic and ballistocardiographic changes after exercise but it was clear that the two were not

necessarily related. Fig. 6 shows the pre- and post-exercise records on a 56-year-old man with a history of angina pectoris of two and one-half years' duration. Both ballistocardiogram and electrocardiogram are normal before exercise. Immediately after exercise the electrocardiogram shows a positive response but the ballistocardiogram remains normal. In contrast are the records shown in Fig. 7 from a 47-year-old man with angina pectoris. The control electrocardiogram and ballistocardiogram are normal. After exercise the ballistocardiogram

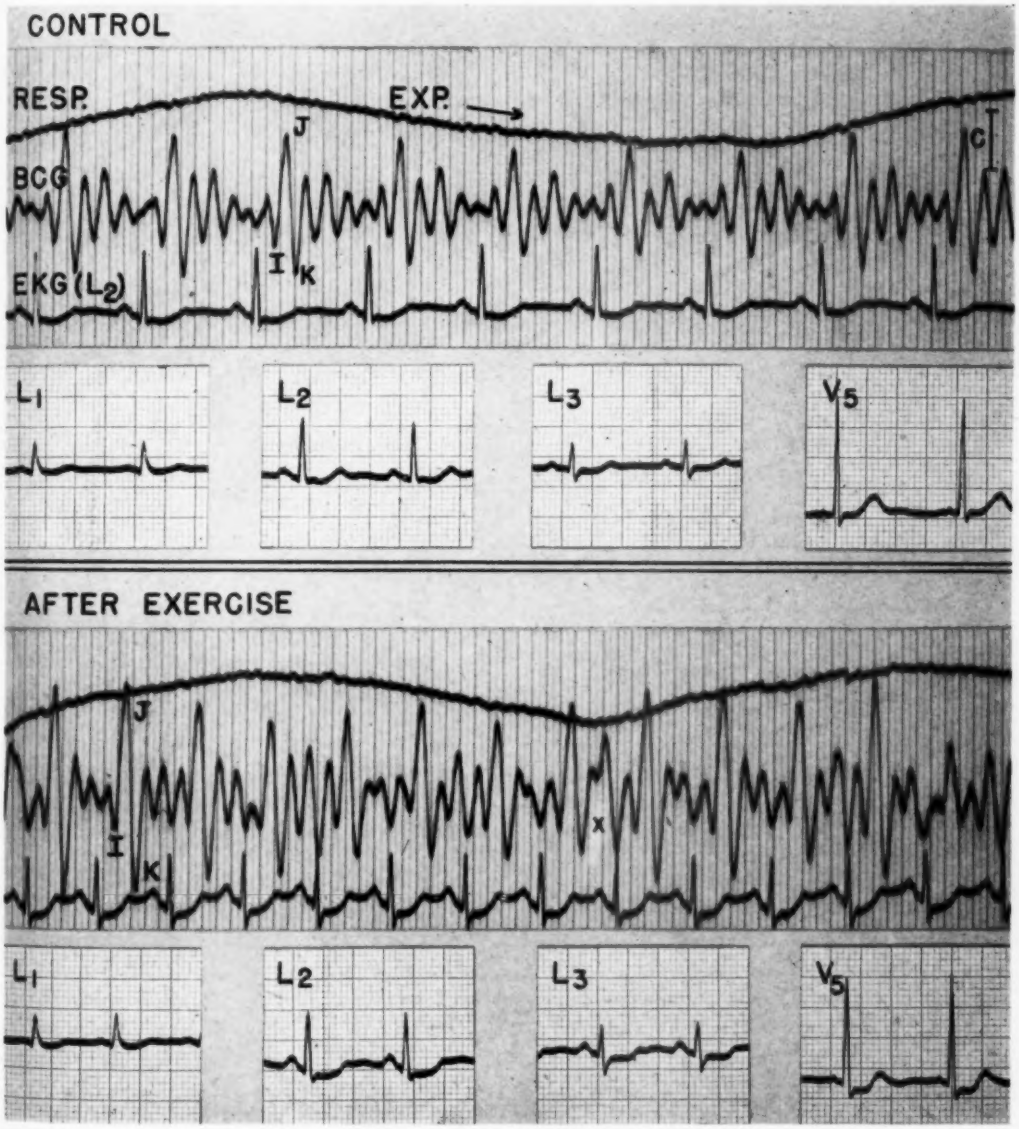


Fig. 6.—A. S., a 56-year-old man with angina pectoris and a normal resting electrocardiogram and ballistocardiogram. After exercise there is a positive Master test but the ballistocardiographic form remains normal and amplitude is considerably increased. Occasionally there is slight distortion of the I wave due to "ride-in." Pneumograph allows identification of respiratory impacts (*X*) which almost invariably occur at the peaks of inspiration and expiration.

becomes abnormal but there is a negative electrocardiographic response. Ballistocardiograms are routinely taken several times over a ten-minute period after the termination of exercise. In some cases there has been improvement in the early post-exercise records with gradual deterioration thereafter followed by a gradual return to the form of the control record. In the early post-exercise ballistocardiograms respiratory artifacts are very frequent and for this reason a

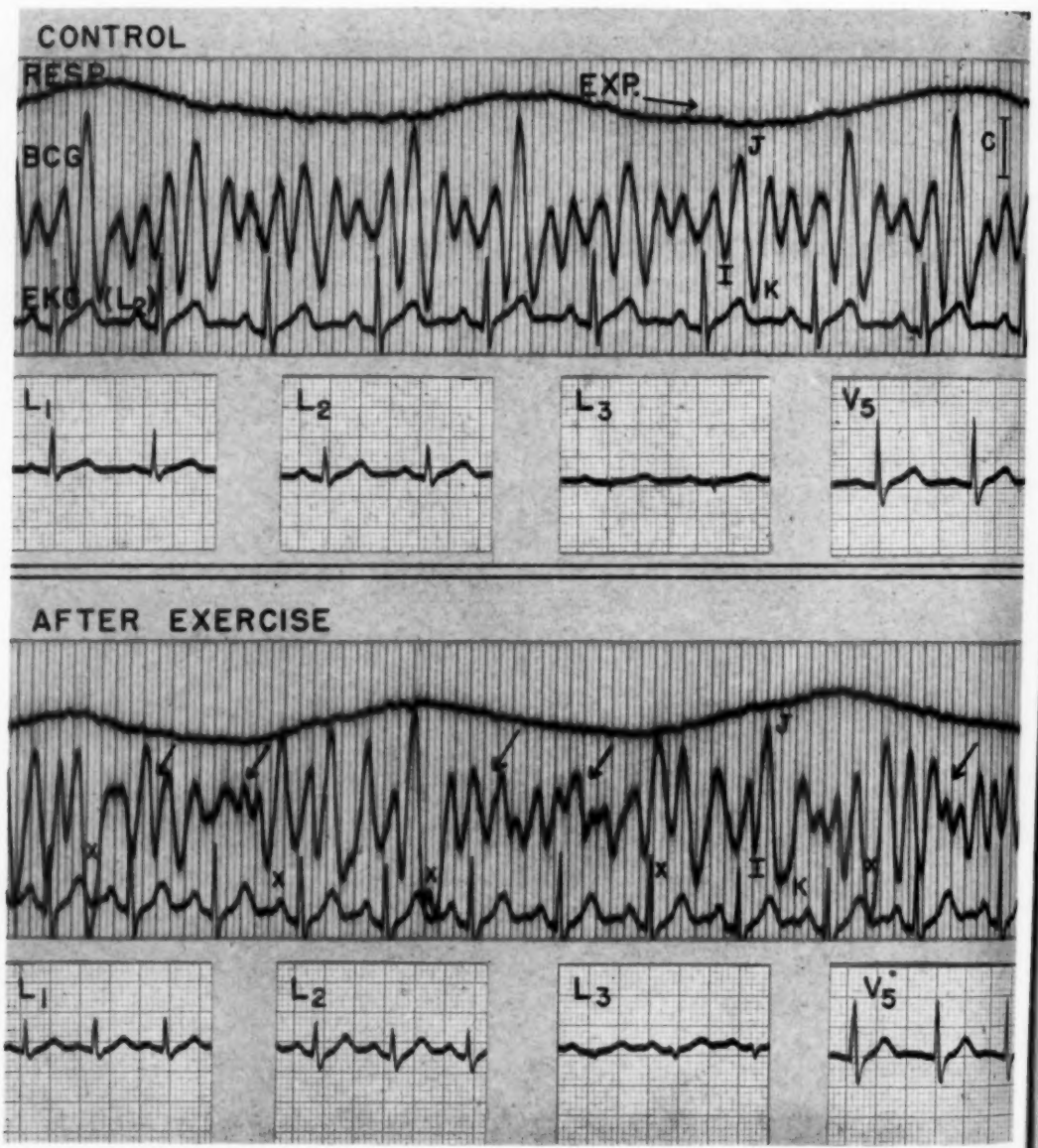


Fig. 7.—R. B., a 47-year-old man with angina pectoris and a normal resting electrocardiogram and ballistocardiogram. After exercise there is a negative Master test but the ballistocardiogram becomes abnormal. Mean IJ amplitude is decreased and about one-half of the complexes are abnormal (arrows); these are not associated with respiratory impacts (*X*).

pneumographic tracing is an almost indispensable aid in the evaluation of these records.

3. *Form abnormalities*: The abnormalities encountered in the records from patients with angina pectoris were similar in kind to those observed in the records from older clinically normal subjects.[4] The ballistocardiographic vector records and the responses to abdominal compression were also similar in patients and normal persons with abnormal head-foot records. Fig. 3,*B*, shows the ballistocardiograms from a 59-year-old patient with diabetes and angina pectoris. The control head-foot record, distinctly abnormal, shows only one or two normal complexes in each respiratory cycle; the remaining complexes are small and abnormal with prominent H waves and small or absent I, J, and K waves. On the other hand the complexes in the 60° Rt. and 90° Rt. vector records are of large amplitude and are entirely "normal" in form. This is a rather remarkable example of an abnormal head-foot record with "normal" vector records. Abdominal compression renders the abnormal head-foot record normal by improving ballistic form, increasing amplitude, and reducing respiratory variation.

Among the patients with angina pectoris were two in whom there was strong evidence for syphilitic aortitis with coronary ostial stenosis. It is of interest that the ballistocardiograms were normal in both. One was a 44-year-old man whose attacks of angina pectoris became so severe and prolonged as to require hospitalization. There were progressive electrocardiographic changes, consistent with acute coronary insufficiency, all of which disappeared before discharge. Ballistocardiograms before, during, and after this episode were all normal. Two months later he died suddenly while in bed. The second was a 55-year-old man whose angina had been present for eight years. Although there was slight cardiac enlargement his ballistocardiogram was normal in form and amplitude.

4. *Summary*: In a group of 191 patients with angina pectoris the ballistocardiogram was abnormal in 75 per cent and the electrocardiogram was abnormal in 24 per cent; in 78 per cent one or both were abnormal. The frequency of abnormal ballistocardiograms was significantly greater than that for abnormal electrocardiograms in all decades except the fourth. Like the findings in the infarction group, there was an increasing incidence of abnormal ballistocardiograms with age in the patients with angina pectoris. Only 54 per cent of the subjects below the age of 50 had abnormal records whereas above 50 the incidence was 84 per cent. The frequency of abnormal ballistocardiograms was significantly higher in the patients with angina pectoris than in normal subjects in the third, fourth, fifth, and sixth decades. By including the results of single "two-step" exercise tests the incidence of electrocardiographic "abnormality" for the whole group was increased from 24 to 57 per cent.

C. Analysis of Normal and Borderline Ballistocardiograms From Patients With Coronary Artery Disease.—In view of the high incidence of normal ballistocardiograms in the younger patients with angina pectoris or old myocardial infarction, a rather extensive analysis was made of the normal and borderline ballistocardiograms in the coronary artery disease group in the hope that sig-

nificant differences might exist between these records and the normal or borderline records from apparently normal persons.

In order to obtain a group of patients with coronary artery disease of sufficient size and similarity to warrant statistical analysis it was necessary to restrict the analysis to the fifty-two men in the fifth and sixth decades with normal (twenty-seven cases) or borderline (twenty-five cases) ballistocardiograms. Some sixty variables were measured in each case and were summarized separately in the normal and borderline groups. The findings in the normal records from the patients with coronary disease were than compared with those in fifty-nine normal records from healthy men in the fifth and sixth decades. The mean value for each of the variables was determined in both groups. Significance was attached to a difference between two means when the difference was greater than twice its standard error (that is, d/S.E. > 2.0). Similarly the borderline records from the coronary artery disease group were compared with the borderline records from twenty-two normal men in the fifth and sixth decades.

The most remarkable result of the analysis was the striking similarity of (1) the normal ballistocardiograms from patients with coronary disease and from normal subjects and of (2) the borderline ballistocardiograms from the same two groups. In the comparison of the normal records the only variable in which there was a significant difference was the ratio JK/IJ. This ratio was significantly smaller in the coronary group and reflected the tendency toward short K waves in these records. Comparison of the borderline records revealed that the only significant difference between the two groups was in the amplitude of the inspiratory J wave which was shorter in the coronary group than in the normal group.

It is concluded that detailed analysis failed to reveal any important differences between the normal records from patients with coronary artery disease and those from normal subjects or between the borderline records from the coronary and normal groups. The consistency of the quantitative results suggests that the original qualitative classification was also consistent.

DISCUSSION

Review of Use of Ballistocardiograph in Coronary Artery Disease.—The use of the ballistocardiograph in the study of patients with coronary artery disease dates back to 1940 when Starr and Schroeder,[8] using their high-frequency bed, noted that each of the three types of abnormal ballistic complexes they described (late downstroke, early M, and late M) were found in patients with coronary arteriosclerosis. In 1943 Starr and Wood[9] reported the results of ballistocardiographic studies on twenty-seven patients with acute myocardial infarction and twenty-eight patients with chronic angina pectoris. Their analysis is the only one which has been reported on quantitative measurements from the records of patients with coronary artery disease. They found that only 26 per cent of the cases of infarction and 18 per cent of the cases of angina pectoris had ballistocardiograms abnormal in form. However, cardiac output and left ventricular

work calculated from the normal records were considerably lower than in those from a group of normal subjects of both sexes between 20 and 40 years of age. Since his earlier studies Starr has changed some of his concepts with regard to what constitutes form abnormality and it is probable that some of the records classified as normal would now be considered abnormal. Starr's change in interpretation has an important bearing on the study under discussion because the "early M" pattern, which was so frequent in his patients with coronary artery disease, was not considered originally a serious form of abnormality. Cardiac output was calculated from records of the "early M" type as well as from others in which abnormal complexes appeared during only a part of the respiratory cycle. (That the low incidence of form abnormality in this study by Starr and Wood may have been due to conservative interpretation is suggested by a more recent study by Starr and Mayock[10] in which it was found that 50 per cent of the cases of angina pectoris and myocardial infarction tested between 1937 and 1947 had abnormal ballistocardiograms.) Starr and Wood compared their patients with coronary artery disease (whose ages were not indicated) with 20- to 40-year-old normal subjects and found that mean cardiac output was 27 per cent lower in the patients than in the normal persons. Inasmuch as cardiac output as calculated from the ballistocardiogram declines with age, had their patients and normal subjects been comparable in age the difference in cardiac output would certainly have been smaller. Cardiac output in our 40- to 59-year-old patients with normal ballistocardiograms was significantly lower than in our 20- to 39-year-old normal persons but was actually slightly higher than in our 40- to 59-year-old normal persons.

One of Starr's early impressions was that the prognosis in patients who had sustained myocardial infarction was better when the ballistocardiogram was normal than when it was abnormal. In 1946 he reported four cases tending to support this view.[11] These patients, who had their infarctions at the ages of 55, 31, 58 and 52, all had normal ballistocardiograms when studied fifteen, seven, seven, and five years later, respectively, and all were active and working. Whether there are similar patients with abnormal ballistocardiograms following infarction who do equally well is not known. Evaluation of the prognostic significance of the ballistocardiogram in patients with coronary artery disease will require a long-range follow-up in order to correlate the ballistocardiographic findings with morbidity and duration of life.

The value of such follow-up studies is amply demonstrated by the results reported by Starr[12] on the future course of ninety apparently normal persons over the age of 40, originally tested between 1937 and 1939. Their after-histories were reviewed in 1947, eight to ten years later. Only four of the ninety persons had ballistocardiograms which were originally abnormal in form. Three of these four developed manifest coronary artery disease during the follow-up period and only one remained healthy over the ten-year period. In addition, of the eighty-six normal control subjects with ballistocardiograms normal in form, the six who had the smallest records in proportion to body weight all developed angina pectoris or myocardial infarction during the follow-up period. Six other patients either died of heart disease or developed clinical coronary artery disease, and in three

of these the ballistocardiogram was smaller than the average for the subject's age group. These findings are of obvious importance for they indicate that the ballistocardiograph was able to detect abnormality of cardiac function before coronary artery disease manifested itself clinically. This does not imply that all persons with ballistocardiograms abnormal in form or small in amplitude will necessarily develop heart disease or that none of the subjects with normal ballistocardiograms will develop it. However, the general relationship between ballistic form and/or amplitude and the later development of heart disease in Starr's group is strongly suggestive. It should be noted that the incidence of abnormal ballistocardiograms in Starr's series of older normal subjects is much lower than in ours and in those of Dock and associates[13] and Taymor and associates.[14] This discrepancy has been commented on elsewhere.[4]

In 1948 Starr and Mayock[10] reported the results of a study of 234 cases with abnormal ballistocardiograms. A summary was made of the frequency of abnormal records in various clinical conditions. The ballistocardiogram was more frequently abnormal in coronary heart disease (angina pectoris or myocardial infarction) than in any of the other varieties of heart disease. Among the 127 patients with coronary artery disease, sixty-three had abnormal records, an incidence of 50 per cent. Fifty-three of the 234 patients with abnormal ballistocardiograms were known to have died at the time of the report, and autopsy data were available on forty of them. It is of interest that the hearts were morphologically normal in only nine of the fifty-three cases and in eight of these the ballistocardiogram was abnormal only immediately after surgical operation. The production of temporary abnormality of form by surgical procedures is well known. Therefore, only the one case with an abnormal ballistocardiogram but an anatomically normal heart remains to be explained. Starr has pointed out that abnormality of the ballistocardiogram and of the morphology of the heart will be related only in so far as anatomic abnormality causes or is associated with abnormality of cardiac ejection. General systemic, metabolic, and endocrine diseases may produce ballistic form abnormality without causing detectable structural damage to the heart.

The recent experimental work by Starr and his associates[15] has made it possible to assign to abnormal ballistocardiograms quantitative physiologic meaning. They found that there is a close relationship between the amplitude of a ballistic complex and the maximum force produced during a given cardiac systole, that is, ballistic IJ amplitude is related to maximum cardiac force. Whereas the calculation of cardiac output requires complexes of normal form, Starr indicates that maximum cardiac force can be calculated from any complex regardless of its form. The application of this method to the normal and borderline records of patients with coronary artery disease was made in our study and no difference in maximum cardiac force was found between these patients and normal subjects in the same age groups with normal or borderline ballistocardiograms.

During the last few years a large number of reports have appeared in the literature on the use of the ballistocardiograph in coronary artery disease. Brown, Hoffman, and deLalla[16] (who used a high-frequency bed) reported twenty-six

cases of typical angina pectoris all of whom had some degree of ballistocardiographic abnormality. The degree of ballistic abnormality appeared to be related both to the presence or absence of clinical cardiac abnormality and to the severity of the disease. It was pointed out that there are a great many patients with coronary sclerosis whose complaints are atypical and it was suggested that the ballistocardiogram may be of diagnostic value in these cases. The authors recommended a system for grading abnormal ballistocardiograms based on respiratory variation and degree of ballistic abnormality. They also devised a method for quantitating the degree of respiratory variation in the ballistocardiogram. Their "Respiratory Variation Index" (R.V.I.) is calculated by dividing the difference between inspiratory and expiratory minute volumes by body surface area, the results being expressed in cubic centimeter per minute per square meter surface area. Normal persons (most of them between 25 and 35 years of age) were found to have values between 0 and 450 but all of twenty-one patients with angina pectoris and Grades I and II abnormal ballistocardiograms had values above 450. They emphasized the significant fact that increased respiratory variation is one of the first manifestations of ballistocardiographic abnormality. However, evidence is presented elsewhere[4] indicating that this index (R.V.I.) is of limited value because of the difficulty in calculating cardiac output from abnormal ballistocardiograms (Brown's Grades I and II) and because of its high degree of variability, which is due largely to variation in cardiac output from one person to the next. The simple ratio of expiratory to inspiratory IJ amplitudes ("Ra," expressed in per cent) was found to be independent of cardiac output, much less variable, and easier to calculate. Inasmuch as there is a progressive increase in respiratory variation with age, caution must be exercised in comparing young normal subjects with middle-aged patients with angina pectoris. Marked respiratory variation with expiratory deterioration is frequently seen in the abnormal ballistocardiograms of older normal persons as well as of patients with coronary artery disease. deLalla and Brown[17] have speculated on the causes of increased respiratory variation and suggested that it might be due to peripheral and splanchnic blood pooling which causes a diminution in the pulmonary pool and a relative decrease in left ventricular output during expiration. This view is supported by their finding that respiratory variation increases following sympathectomy and decreases when peripheral and splanchnic pooling is reduced by pressure from elastic stockings or an abdominal binder. They believe that in certain cases coronary insufficiency may be secondary to a critically low left ventricular output caused by increased peripheral pooling. This is in accord with the view held by Kerr and associates[18] as a result of their observation that patients with angina pectoris were frequently improved symptomatically while wearing an abdominal support. In an effort to determine whether there was symptomatic improvement in those patients with coronary artery disease whose ballistocardiograms improved while wearing an abdominal support, Brown and associates[19] selected forty patients to wear a special abdominal support and followed them closely for eighteen months. The results were impressive, for 92 per cent of the group showed definite symptomatic improvement and increase in exercise tolerance. Thus they were able to show that abdominal support produced

improvement in symptoms as well as in ballistocardiographic form. Their forty patients represented only 15 per cent of a larger group of 250 patients, 85 per cent of whom failed to show ballistocardiographic improvement with abdominal compression. McCann[20] pointed out that an abdominal belt frequently fails to relieve patients with angina pectoris and may even increase their symptoms. He suggested that the effectiveness of an abdominal support in such patients may be a matter of the optimal amount of compression which facilitates the transfer of blood from the abdomen to the chest without at the same time impeding the return of blood from the legs. This suggestion, which seems a logical one, is supported by studies from this laboratory indicating that there is a critical pressure level (which varies from person to person) beyond which ballistocardiographic form invariably deteriorates. Further work is needed before the value of abdominal supports in the treatment of patients with angina pectoris can be established. This work should aim at determining the optimal pressure level for the individual subject and at securing objective evidence for the improvement in cardiovascular function due to abdominal compression. In addition, the identification of the mechanisms through which abdominal compression produces improvement in symptoms and in the ballistocardiogram is of great importance.

The effect of the ingestion of food on the electrocardiograms and ballistocardiograms of patients with angina pectoris has been studied by Berman, Braunstein, and McGuire.[21] Ballistocardiograms, recorded with a high-frequency bed, were taken before and thirty minutes following a standard meal in twenty-three patients. Only five (22 per cent) had sufficiently normal control records to allow the calculation of cardiac output. Following the meal the cardiac output of the patients decreased an average of 4 per cent while that of normal subjects increased an average of 24 per cent. Eighteen of the twenty-three patients (78 per cent) had abnormal control ballistocardiograms which precluded the calculation of cardiac output. After the meal amplitude increased slightly in four of these, decreased in three, and was unchanged in eleven. These findings suggest that patients with angina pectoris are unable to increase their cardiac outputs following the ingestion of food in the same way that normal individuals do.

The effect of anoxemia on the high-frequency ballistocardiograms of a group of patients with angina pectoris has been reported by Scarborough and his associates.[22] The few patients whose records allowed the calculation of cardiac output and related variables showed the same type of response as a larger group of normal subjects did. Both normal subjects and patients increased their cardiac outputs about 40 per cent when arterial saturation was decreased to 70 per cent. As a consequence of anoxemia one normal, one abnormal, and two borderline ballistocardiograms from the patients became abnormal or more abnormal.

In all of the ballistocardiographic studies, referred to above, the Starr-type high-frequency bed was employed. The Nickerson[23] low-frequency, critically damped bed has not as yet received extensive use in the study of patients with coronary artery disease. Mathers and associates[24] studied four patients with coronary sclerosis, three of whom showed abnormal ballistocardiograms which improved after digitalis administration. It is of interest that one of these was not in cardiac failure and his only abnormality was a bowed JK segment; fol-

lowing intravenous lanatoside C there was prompt straightening of the JK segment. Oral digitalization had no apparent influence on the record of the single patient whose control ballistocardiogram was normal. In another study by Mathers and associates,[25] observations were made on the effect of ascending an ordinary flight of steps by five normal subjects and five patients with coronary heart disease. Observations were made of pulse rate, cardiac work, cardiac output, and pulse pressure before and after ascending and descending a flight of steps and walking on level ground. The responses of the patients to the standard effort were not significantly different from those of the normal subjects. It was concluded that patients with coronary heart disease may climb stairs at their own pace without imposing a greatly increased burden of work on the heart.

In 1949 Dock and Taubman[26] reported several techniques which allow the recording of the ballistocardiogram directly from the body. The most satisfactory of these is a photoelectric method, which records the displacement of the body, and an electromagnetic method, which records the velocity of body motion. With each technique records are made from the shins while the floor or a rigid table serves as reference for the motion. Later Sheehan and associates[27] described a piezoelectric direct-body pickup which, like the photoelectric, records body displacement. The wave form of the ballistocardiograms recorded with these direct-body pickups from normal subjects is roughly similar to that recorded by the high-frequency bed. No satisfactory method has been devised for the mechanical calibration of these instruments and for this reason interpretation is based solely on qualitative analysis of the records.

Since the introduction of the direct-body pickups a number of reports have appeared on their application to the study of patients with coronary artery disease. They have been used by Dock to study a wide variety of cardiovascular problems. He noted that men under the age of 35 who have recovered from myocardial infarction may show normal ballistocardiograms but that older men may show bizarre records as the first objective sign of coronary disease. In acute myocardial infarction he found that low amplitude, bizarre ballistic complexes may precede electrocardiographic changes.[26] Several reports have appeared in the literature by Dock and associates[13] and by Mandelbaum and Mandelbaum[28, 29] on ballistocardiography in patients with coronary artery disease. These investigators have studied large groups of patients as well as normal subjects. Ballistocardiograms (electromagnetic) were recorded before and after standard exercise and the records were evaluated using the classification of Brown and his associates[16] or a modification of it. Since post-exercise ballistocardiograms were included in the evaluation of the subjects in their studies, our results are not directly comparable with theirs. Nevertheless there are striking similarities in the findings. This is particularly true of the normal subjects, for if all grades of abnormal records in their study are combined and compared with our "abnormal" records, the curves relating ballistic abnormality to age are almost superimposable. The rapidly increasing incidence of abnormality above the age of 40 years is clearly evident in both studies. This same age trend is also present in their patients with angina pectoris and myocardial infarction but the trend is not as decided as in our groups. Combining all degrees of abnormality they found

abnormal records in approximately 85 per cent of their 30- to 40-year-old patients with coronary artery disease whereas we found only 40 per cent. (Combining our borderline and abnormal records produces figures more closely resembling theirs.) Mandelbaum and Mandelbaum summarized their findings in 224 patients with angina pectoris by stating that about 11 per cent had normal ballistocardiograms at rest (which compares with our 12 per cent) but less than 1 per cent had normal records after exercise. The increase in frequency of abnormal records after exercise was noted in their normal subjects as well as in their patients with angina pectoris. The results obtained by these workers are quite impressive, and it is hoped that a long-term follow-up will be made on their patients.

Gubner and associates[30,31] have used the photoelectric pickup in the study of a large group of clinically normal persons as well as of some patients with coronary artery disease. Gubner noted that important changes in the ballistocardiograms of older normal individuals occur very frequently. Among these changes were: an increase in respiratory variation, relatively tall H waves, short I waves, low often slurred J waves (which appeared late), deep and early K waves, and prominent L waves. One portion of Gubner's study was concerned with the detection of arteriosclerosis in a group of 320 individuals over a wide age span by means of radiologic and electrocardiographic methods. His results clearly showed the rising incidence of arteriosclerosis with age. Evidence of arteriosclerosis was present in 18 per cent of subjects 36 to 40 years of age and its frequency increased to a peak of 79 per cent in subjects 61 to 65 years of age. These results are similar in kind to those reported by White, Edwards, and Dry[32] on the increasing frequency of severe coronary artery sclerosis with age. The parallel between the increasing frequency of arteriosclerosis and of abnormal ballistocardiograms with age is apparent.

Pordy, Taymor, Moser, Chesky, and Master,[33] using the photoelectric direct-body pickup, studied eighty normal subjects between the ages of 18 and 64 years. Records were classified in normal, borderline, and abnormal categories on the basis of the wave form. Below the age of 50 there were abnormal records in 4.5 per cent of the cases and above the age of 50 there were abnormal records in 14 per cent. The incidence of abnormal records in their older group is much lower than in Mandelbaum's and ours but this may be due in part to the small number of older subjects studied. Of the eighty subjects, standard exercise ("two-step" test) rendered three normal and two borderline records abnormal. More recently this group (Taymor and associates[14,34]) reported the results of a study correlating the ballistocardiogram with the electrocardiographic response to the Master two-step test in 195 patients. The patients were divided into three groups according to the electrocardiographic results of the Master test; the frequency of abnormal, borderline, and normal ballistocardiograms (before and after exercise) in each group was determined. Although there were a few patients with typical angina pectoris in the negative two-step group and a few asymptomatic subjects in the positive two-step group, for practical purpose those with positive tests were symptomatic and those with negative tests were not. In the group with negative two-step tests the resting ballistocardiogram was abnormal in 16 per cent, and after exercise this figure increased to 24 per cent; the records were

abnormal before or after exercise in 37 per cent of the subjects above the age of 50. On the other hand, in the group with positive two-step tests the resting ballistocardiogram was abnormal in 83 per cent and after exercise this figure increased to 93 per cent. Before exercise there were *normal* ballistocardiograms in 12 per cent of this group and after exercise in only 1.3 per cent. These figures are almost identical with Mandelbaum's (resting, 11 per cent; after exercise, less than 1 per cent) and with ours (resting only, 12 per cent) in patients with angina pectoris. These three studies employing different ballistocardiographic methods and involving only qualitative evaluation of the records are surprisingly consistent. The reason for the disparity between these results and those reported by Starr and Wood[9] earlier is not clear. Starr and Mayock[10] reported the frequency of abnormal ballistocardiograms from 556 individuals above the age of 50, with and without cardiac disease. Abnormal records were found in only 24 per cent of this large group, an incidence much lower than we found in our clinically normal persons above 50. A comparison of interpretations in a small number of records failed to reveal any significant differences between Starr's interpretation of records and our own.

Comment on Results.—This study revealed that 74 per cent of 328 patients with angina pectoris or old myocardial infarction had abnormal ballistocardiograms at rest; the records were normal in 13 per cent and borderline in the remainder. Electrocardiograms were abnormal in 56 per cent of the whole group, in 24 per cent of the patients with angina pectoris, and in 69 per cent of the patients with old myocardial infarction.

One of the most important findings was the rather small proportion of young patients with coronary artery disease who had abnormal ballistocardiograms. In the age group, 30 to 39 years, only 38 per cent of the patients with myocardial infarction and 45 per cent of the patients with angina pectoris had abnormal ballistocardiograms. The slope of the line relating the incidence of abnormality to age for the patients is similar to that for normal subjects. The findings in these two groups point up the importance of taking age into consideration when results of ballistocardiographic studies are being evaluated. It should be emphasized that in the age groups in which the incidence of ballistic abnormality is low for normal subjects it is also low for patients with coronary artery disease. Conversely, in those age groups in which abnormal ballistocardiograms are frequent in coronary artery disease they are also frequent in apparently normal persons. This is particularly well shown in patients with angina pectoris in the eighth decade for, although all of them had abnormal records, 92 per cent of the normal subjects in the same age group also had abnormal ones. It is apparent then that the ballistocardiographic differences between patients with coronary artery disease and normal subjects are quantitative and not qualitative, since clinically normal persons may have abnormal records and patients with coronary artery disease may have normal ones. These findings suggest that significance should be attached to *abnormal* ballistocardiograms from subjects below the age of 50 and to *normal* ballistocardiograms from those above the age of 60. The significance of records which do not fall into these two groups remains to be determined. The problem of the patient in the fifties with an atypical variety of chest pain is a

perplexing one, for if we assume that the pain is of coronary artery origin there are two chances in ten that his record will *not* be abnormal and if we assume the pain to be noncardiac in origin there are three chances in ten that this record will be abnormal. It is possible that the use of stress tests and other physiologic manuevers will further widen the gap between patients with coronary disease and "normal" individuals. These tests are now being employed in both groups and the results will be described at a later date.

There is little doubt that ballistic abnormality is associated with coronary artery disease but at the present time it seems premature to assume that the abnormal ballistocardiograms occurring so frequently in apparently normal subjects over 50 are due to coronary artery disease alone and therefore indicate a serious prognosis. The effect on the ballistocardiogram of physiologic aging of both the heart and the rest of the circulatory system cannot be excluded. Until it is possible to establish a unique or characteristic relationship between coronary artery disease and the ballistocardiogram, one should reserve judgment regarding the significance of abnormal records in clinically normal persons and in patients whose symptoms are not typical of coronary artery disease. Long-term follow-up studies such as those being conducted by Starr should serve to verify the diagnostic and prognostic value of the ballistocardiogram.

SUMMARY

1. One hundred thirty-seven cases of old myocardial infarction and one hundred ninety-one cases of angina pectoris were studied by both ballistocardiography and electrocardiography. Results were compared with those from a similar study of three hundred sixty-nine clinically normal subjects.

2. Sixty-nine per cent of patients with old myocardial infarction had abnormal electrocardiograms and 72 per cent had abnormal ballistocardiograms. The incidence of abnormal electrocardiograms and ballistocardiograms was significantly higher in each age decade for the patients with old myocardial infarction than for the normal subjects. There was an increasing frequency of ballistic abnormality with age, ranging from 38 per cent in the fourth decade to 96 per cent in the seventh decade.

3. Twenty-four per cent of patients with angina pectoris had abnormal electrocardiograms whereas 75 per cent of them had abnormal ballistocardiograms. The percentage of abnormal ballistocardiograms was significantly higher than that for abnormal electrocardiograms in the fifth, sixth, seventh, and eighth decades. There was an increasing frequency of ballistic abnormality with age, ranging from 45 per cent in the fourth decade to 100 per cent in the eighth decade. In a small group of patients with normal or borderline ballistocardiograms and electrocardiograms, the "two-step" exercise test produced ballistic abnormality in 60 per cent, and a positive electrocardiographic response in 30 per cent.

4. Detailed quantitative analysis of the normal and borderline ballistocardiograms from normal subjects and from patients with coronary artery disease failed to reveal any important differences between the two clinical groups.

5. In the age groups in which the incidence of ballistic abnormality was low for clinically normal subjects it was also low for patients with coronary artery

disease, and in those age groups in which the incidence of ballistic abnormality was high for patients with coronary artery disease it was also high for clinically normal subjects. It is suggested that significance be attached to abnormal ballistocardiograms from subjects under the age of 50 and to normal ballistocardiograms from those over the age of 60.

6. It is recommended that, for the present, caution be used in attributing clinical significance to abnormal ballistocardiograms from clinically normal persons and from patients whose symptoms and signs are not typical of coronary artery disease.

7. The literature is reviewed with respect to the use of ballistocardiography in coronary artery disease.

REFERENCES

1. Heberden, W.: Some Account of a Disorder of the Breast, Med. Trans. Royal Coll. Physicians **2**:58, 1772.
2. Starr, I., Rawson, A. J., Schroeder, H. A., and Joseph, N. R.: Studies on the Estimation of Cardiac Output in Man and of Abnormalities in Cardiac Function From the Heart's Recoil and the Blood's Impact, Am. J. Physiol. **127**:1, 1939.
3. Baker, B. M., Jr., Scarborough, Wm. R., Mason, R. E., and Singewald, M. L.: Coronary Artery Disease Studied by Ballistocardiography. A Comparison of Abnormal Ballistocardiograms and Electrocardiograms, Tr. Am. Clin. & Climatol. **62**:191, 1950.
4. Scarborough, Wm. R., Davis, F. W., Jr., Baker, B. M., Jr., Mason, R. E., Singewald, M. L., Lore, S. A., and Fox, L. M.: A Ballistocardiographic Study of 369 Apparently Normal Persons: An Analysis of "Normal" and "Borderline" Ballistocardiograms. In publication.
5. Yater, W. M., Traum, A. H., Brown, W. G., Fitzgerald, R. P., Geisler, M. A., and Wilcox, B. B.: Coronary Artery Disease in Men 18 to 39 Years of Age: Report of 866 Cases, 450 With Necropsy Examination, Am. Heart J. **36**:334, 481, and 683, 1948.
6. Scarborough, Wm. R., Beser, J., Talbot, S. A., Mason, R. E., Singewald, M. L., and Baker, B. M., Jr.: A Method for Recording Ballistocardiographic Vectors. Preliminary Report, Bull. Johns Hopkins Hosp. **87**:235, 1950.
7. Pordy, L., Master, A. M., and Chesky, K.: Value of Cardiac Function Tests in Industry, J. A. M. A. **148**:813, 1952.
8. Starr, I., and Schroeder, H. A.: Ballistocardiogram. II. Normal Standards, Abnormalities Commonly Found in Diseases of the Heart and Circulation and Their Significance, J. Clin. Investigation **19**:437, 1940.
9. Starr, I., and Wood, F. C.: Studies With the Ballistocardiograph in Acute Cardiac Infarction and Chronic Angina Pectoris, Am. Heart J. **25**:81, 1943.
10. Starr, I., and Mayock, R. L.: On the Significance of Abnormal Forms of the Ballistocardiogram. A Study of 234 Cases With 40 Necropsies, Am. J. M. Sc. **215**:631, 1948.
11. Starr, I.: Further Clinical Studies With the Ballistocardiograph; on Abnormal Form, on Digitalis Action, in Thyroid Disease and in Coronary Heart Disease, Tr. A. Am. Physicians **59**:180, 1946.
12. Starr, I.: On the Later Development of Heart Disease in Apparently Healthy Persons With Abnormal Ballistocardiograms. Eight to Ten Year After-histories of 90 Persons Over 40 Years of Age, Am. J. M. Sc. **214**:233, 1947.
13. Dock, Wm., Mandelbaum, H., and Mandelbaum, R. A.: Ballistocardiography in Medical Practice, J. A. M. A. **146**:1284, 1951.
14. Taymor, R. C., Pordy, L., Chesky, K., Moser, M., and Master, A. M.: The Ballistocardiogram in Coronary Artery Disease, J. A. M. A. **148**:419, 1952.
15. Starr, I., Horwitz, O., Mayock, R. L., and Krumbhaar, R. N.: Standardization of the Ballistocardiogram by Simulation of the Heart's Function at Necropsy: With a Clinical Method for the Estimation of Cardiac Strength and Normal Standards for It, Circulation **1**:1073, 1950.
16. Brown, H. R., Jr., Hoffman, M. J., and deLalla, V., Jr.: Ballistocardiographic Findings in Patients With Symptoms of Angina Pectoris, Circulation **1**:132, 1950.
17. deLalla, V., Jr., and Brown, H. R., Jr.: Respiratory Variation of the Ballistocardiogram, Am. J. Med. **9**:728, 1950.
18. Kerr, W. J., Cannon, E. F., and Logen, J. B.: A New Approach to the Etiology and Treatment of Angina Pectoris, Tr. A. Am. Physicians **54**:15, 1939.

19. Brown, H. R., Jr., Hoffman, N. J., Epstein, M. A., and deLalla, V., Jr.: The Use of Abdominal Supports in Patients With Angina Pectoris as Selected by the Ballistocardiogram, J. Clin. Investigation **29:**799, (abstract) 1950.
20. McCann, W. S.: Some Neglected Aspects of Cardiology. Circulatory Function of the Respiration, Am. J. Med. **8:**62, 1950.
21. Berman, B., Braunstein, J., and McGuire, J.: The Effect of Meals on the Electrocardiogram and the Ballistocardiogram in Patients With Angina Pectoris, Circulation **1:**1017, 1950.
22. Scarborough, Wm. R., Penneys, R., Thomas, C. B., Baker, B. M., Jr., and Mason, R. E.: The Cardiovascular Effect of Induced Controlled Anoxemia. A Preliminary Ballistocardiographic Study of Normal Subjects and a Few Patients With Suspected Coronary Artery Disease, Circulation **4:**190, 1951.
23. Nickerson, J. L., and Curtis, H. J.: The Design of the Ballistocardiograph, Am. J. Physiol. **142:**1, 1944.
24. Mathers, J. A. L., Nickerson, J. L., Fleming, T. C., and Patterson, M. C.: Abnormal Ballistocardiographic Patterns in Cardiovascular Disease as Recorded With the Low-frequency Critically-damped Ballistocardiograph, Am. Heart J. **40:**390, 1950.
25. Mathers, J. A. L., Griffeath, H. I., Levy, R. L., and Nickerson, J. L.: Effect of Ascending an Ordinary Flight of Stairs on the Work of the Heart. Observations on Normal Individuals and on Patients With Coronary Heart Disease, Circulation **3:**224, 1951.
26. Dock, W., and Taubman, F.: Some Technics for Recording the Ballistocardiogram Directly From the Body, Am. J. Med. **7:**751, 1949.
27. Sheehan, G. A., Jr., Priebe, F. K., Dranetz, A. I., and Howatt, G. N.: A New Pickup for Ballistocardiography, Bull. New York Acad. Med. **26:**262, 1950.
28. Mandelbaum, H., and Mandelbaum, R. A.: Studies Utilizing the Portable Electromagnetic Ballistocardiograph. I. Abnormal HIJK Patterns in Hypertensive and Coronary Artery Heart Disease, Circulation **3:**663, 1951.
29. Mandelbaum, H., and Mandelbaum, R. A.: Clinical Findings With the Dock Ballistocardiograph, New York State J. Med. **15:**1734, 1951.
30. Gubner, R.: The Diagnosis of Arteriosclerosis. Including Observations on Lipid Metabolism and the Ballistocardiogram, Assoc. of Life Insurance Medical Directors of America, October 19-20, 1950.
31. Gubner, R., Rodstein, M., and Ungerleider, H. E.: The Ballistocardiogram: Normal Standards and Determinants of the Waves, Proceedings 23rd. Scientific Session, Am. Heart Assoc., San Francisco, Calif., June 24, 1950.
32. White, N. K., Edward, J. E., and Dry, T. J.: The Relationship of the Degree of Coronary Atherosclerosis With Age in Men, Circulation **1:**645, 1950.
33. Pordy, L., Taymor, R. C., Moser, M., Chesky, K., and Master, A. M.: Clinical Evaluation of the Ballistocardiogram. I. Normal Subjects, Am. Heart J. **42:**321, 1951.
34. Taymor, R. C., Moser, M., Chesky, K., Pordy, L., and Master, A. M.: Clinical Ballistocardiography; Experience in 400 Consecutive Cases, Bull. New York Acad. Med. **27:**385, 1951.

THE HEMODYNAMIC PATTERN IN TRICUSPID VALVE DISEASE

MALCOLM C. MCCORD, M.D.,* AND S. GILBERT BLOUNT, JR., M.D.

DENVER, COLO.

THE UNDERSTANDING of the altered hemodynamics affected by various forms of acquired heart disease has been augmented considerably by information derived from cardiac catheterization. However, knowledge of the pressure changes in the right side of the heart resulting from abnormalities of the tricuspid valve remains incomplete. Bloomfield and associates,[1] Richards,[2] and Werko and Lagerlof[3] have described pressure curves from the right side of the heart secondary to functional tricuspid insufficiency. To our knowledge, no studies have been presented describing the abnormal pressures in organic tricuspid disease. For this reason, an analysis of these changes in the right side of the heart in patients with tricuspid valve disease is presented.

MATERIAL AND METHODS

Four patients with rheumatic valvular heart disease form the basis of this report. All presented clinical evidence of tricuspid regurgitation. The patients were evaluated clinically and by electrocardiography, roentgenography, and by cardiac catheterization. Cardiac catheterization was carried out in the usual manner as described by Cournand and Ranges.[4]

The pressures were measured using Statham strain gauges and a five-channel Hathaway recording apparatus. The reference point used was 10 cm. above the patient's back.[5] The oxygen content of the blood samples was determined by the Van Slyke-Neill method.[6]

RESULTS

CASE 1.—The patient was a 48-year-old white man with a history of symptoms suggestive of active rheumatic fever during adolescence. Cardiac murmurs had been noted for twenty-nine years, and the patient had been aware of pulsating neck veins for twenty years. Ascites first appeared five years ago, followed two years later by exertional dyspnea and dependent edema. Physical examination revealed mild icterus, ascites, and dependent edema. Striking expansile systolic pulsations were noted in the deep cervical neck veins. The heart was greatly enlarged; the lungs were clear. Systolic and diastolic murmurs were audible over the apical area and, with slightly different quality, at the tricuspid area. The liver edge was palpated 10 cm. below the right costal margin and moved downward with each cardiac systole. Atrial fibrillation, with frequent premature ventricular systoles, was present.

From the Cardiovascular Pulmonary Laboratory, University of Colorado School of Medicine, Denver.

This study was supported by a grant (H-241) from the United States Public Health Service.

Received for publication July 3, 1952.

*Postdoctorate Public Health Service Research Fellow of the National Heart Institute.

Physiologic Studies.—The right ventricular pressure curve (Fig. 1) shows an elevated systolic level of 58 mm. Hg. The onset of this wave occurs 0.08 second following the onset of the preceding dominant QRS complex. The wave reaches an initial peak in 0.08 second. The summit of the ventricular pressure wave shows a consistent notching or slurring. Following this notching there is an abrupt fall in pressure in early diastole to levels of from 7 to 14 mm. Hg. Following this dip there is an immediate rise to a sustained level of 25 mm. Hg during the remainder of diastole. Irregular oscillations of low amplitude are consistently present during this plateau period of diastole.

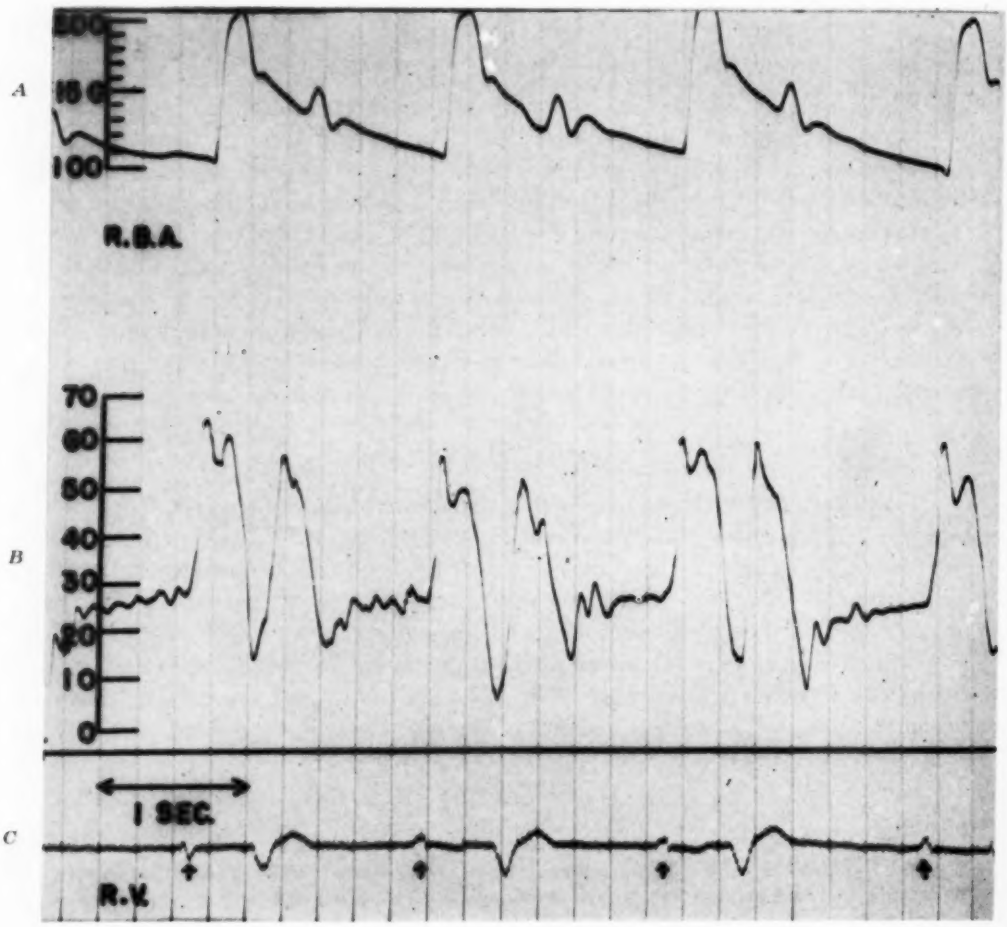


Fig. 1 (Case 1).—*A*, Brachial artery pressure curve. *B*, right ventricular pressure curve. *C*, The electrocardiogram shows atrial fibrillation with coupled ventricular premature systoles. The arrows indicate the dominant conducted QRS complexes. No P waves are present.

The right atrial pressure curve (Fig. 2) shows a systolic level of 50 mm. Hg. The interval from the onset of the preceding QRS complex to the onset of the pressure wave is the same as that in the right ventricle, namely, 0.08 second. There is considerable delay, however, in the time interval from the onset of the systolic wave to the summit. This interval varies from 0.30 to 0.35 second. There is no consistent early diastolic dip in the atrium corresponding to that in the ventricle. The low amplitude oscillations are noted again.

The contour of the pressure wave recorded from the inferior vena cava (Fig. 3) is essentially the same as that in the right atrium. A similar curve was also recorded from the superior vena cava, the left subclavian vein, and from the left brachial vein. Following exercise the pressure in the right atrium rose to a level of 58/32 mm. Hg.

The resting peripheral arterial blood oxygen saturation in this patient was 89 per cent and rose slightly on exercise to 90 per cent. The resting cardiac index was 1.89 liters and showed a rise to 2.26 liters on exercise. The arteriovenous oxygen difference was 7.43 volumes per cent at rest and 8.55 volumes per cent following exercise.

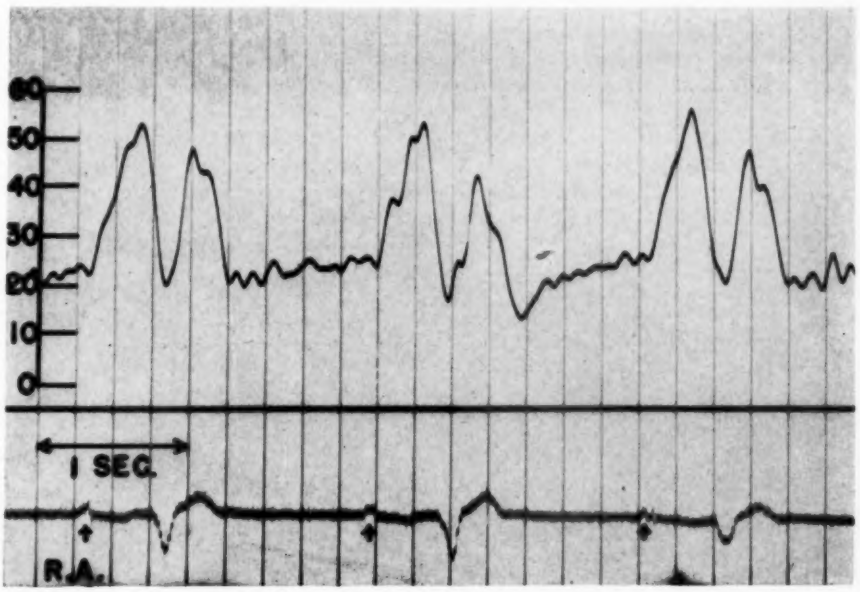


Fig. 2 (Case 1).—Right atrial pressure tracing. The complexes of the electrocardiogram are as described in Fig. 1.

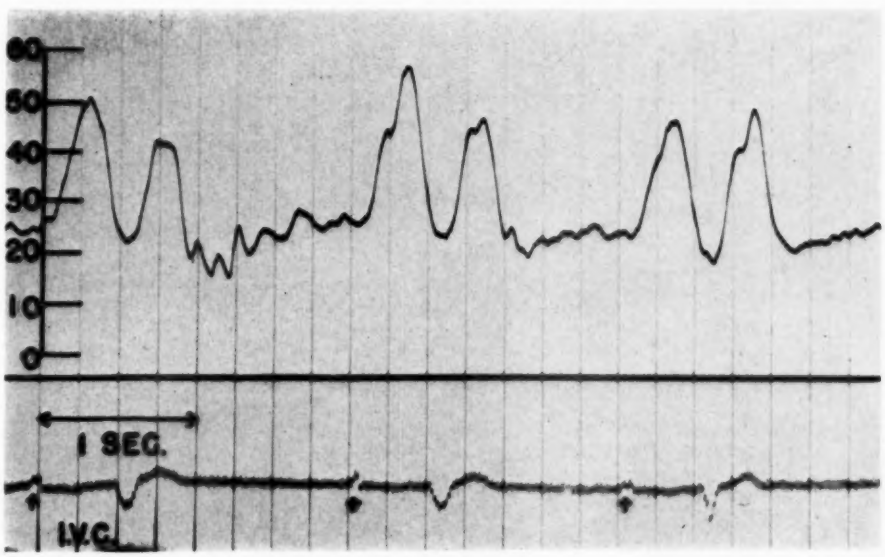


Fig. 3 (Case 1).—Pressure tracing recorded from the inferior vena cava. Electrocardiogram as in Fig. 1.

CASE 2.—A 24-year-old white man presented a history of cardiac murmurs for eighteen years, beginning after scarlet fever. An episode of acute rheumatic polyarthritis occurred ten years ago. Four years ago ascites appeared and two months later exertional dyspnea, cough, dependent edema, and visibly pulsating neck veins were noted. Jaundice, ascites, and dependent edema were observed on physical examination. A wide amplitude pulsation was apparent in the deep neck veins bilaterally during systole. Atrial fibrillation was present. The heart was greatly enlarged and the lungs were clear. Systolic and diastolic murmurs were present at the apex and there was a variation in the murmurs in the fourth intercostal space to the left of the sternum.

Physiologic Studies.—At cardiac catheterization the catheter could be advanced only as far as the right ventricular inflow region. The pressure tracings obtained from the right ventricle (Fig. 4) show a systolic wave having its onset 0.07 second following the QRS complex and reaching an initial peak of 60 mm. Hg in 0.15 second. An exaggerated notching follows, with a second peak of lesser amplitude. The second peak is followed by a rapid pressure decline to levels of 3 to 11 mm. Hg. This is followed by an abrupt rise to a plateau level of 24 mm. Hg in those cardiac cycles with a long diastolic phase. Small amplitude oscillations are noted during this diastolic phase.

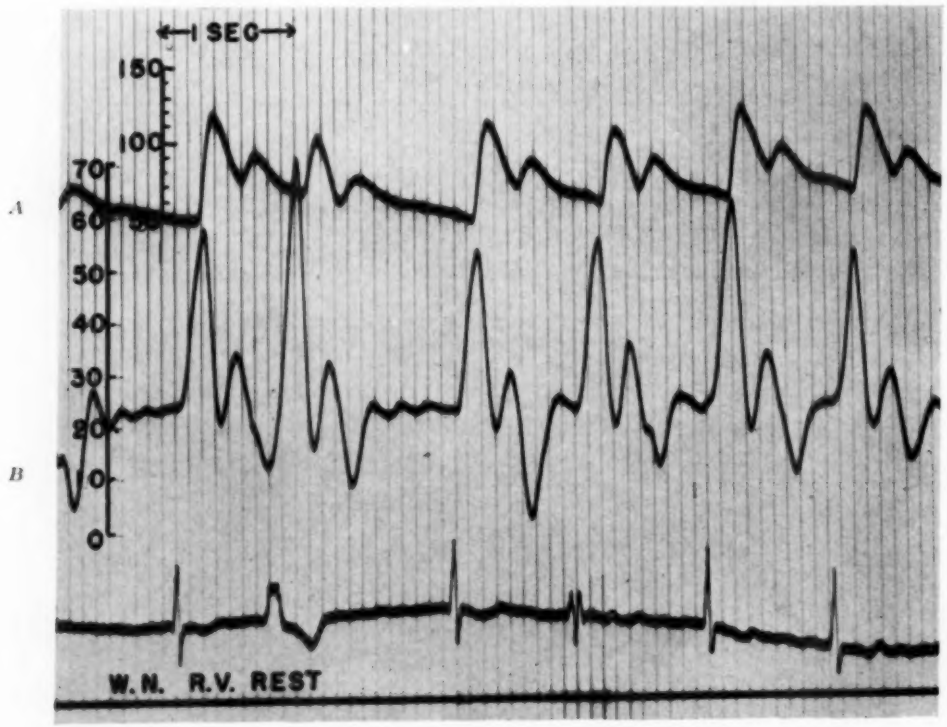


Fig. 4 (Case 2).—*A*, Right brachial artery. *B*, Right ventricular pressure curve.

The atrial pressure at rest (Fig. 5) rises during systole, reaching a level of 30 mm. Hg late in systole. The onset of the wave has the same time relationship to the preceding QRS complex as does the systolic wave in the right ventricle. The summit of the systolic wave in the atrium is not reached until 0.35 second after its onset. Following the systolic peak there is a fall in pressure to levels of 12 to 15 mm. Hg. The notching seen in the atrial curve corresponds to that noted in the ventricular wave. Following exercise there is marked alteration in the contour of the atrial pressure wave (Fig. 6). There is a rise in the pressure to levels of 60/26 mm. Hg, and the contour resembles a ventricular pressure curve. A delay from the onset of the systolic wave to its crest persists.

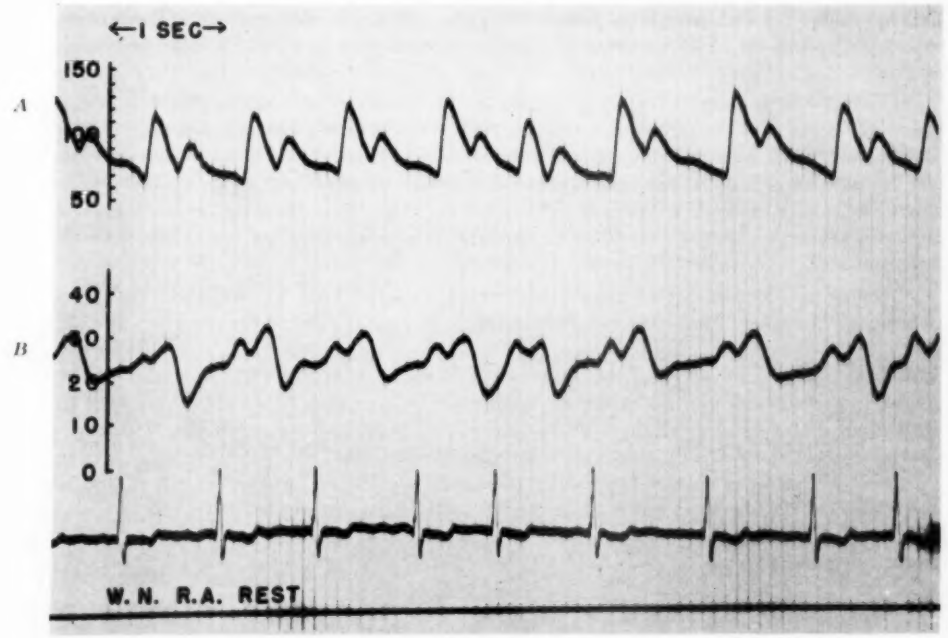


Fig. 5 (Case 2).—*A*, Right brachial artery. *B*, Right atrial pressure curve at rest.

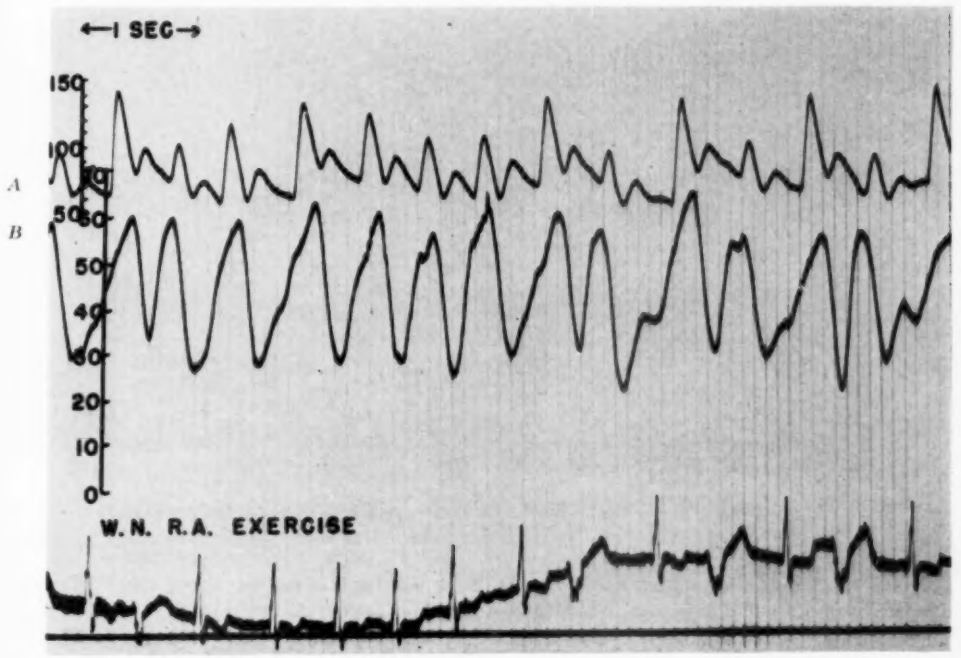


Fig. 6 (Case 2).—*A*, Right brachial artery. *B*, Right atrial pressure curve immediately following exercise.

The resting cardiac index in this patient was 1.90 liters. Following exercise the index increased slightly to 2.17. The peripheral arterial oxygen saturation was normal. The arteriovenous oxygen difference was 7.84 volumes per cent at rest, increasing to 10.98 volumes per cent after exercise.

CASE 3.—A 12-year-old white boy had rheumatic fever with polyarthritis at the age of 6 years. Cardiac murmurs were described at this time. Chorea was manifest at 7 years of age. Dependent edema was first noted at 10 years of age. Examination disclosed systolic pulsations of moderate amplitude in the neck veins, hepatic enlargement, and bulging of the precordium. The heart was considerably enlarged. A loud systolic murmur was heard at the apex and at the tricuspid area. A low rumbling diastolic murmur was audible over the apical area and also in the tricuspid area. Normal sinus rhythm was present.

Physiologic Studies.—The pulmonary artery pressure was 119/60 mm. Hg. The mean pulmonary "capillary" pressure was 26 mm. Hg. The right ventricular pressure was 123/1, and the right atrial pressure (Fig. 7) shows an elevated level of 25/15 mm. Hg. A small wave is seen with an onset 0.17 second after the onset of the P wave of the electrocardiogram. This wave is considered to result from atrial contraction. A larger wave follows, having its onset 0.16 second after the onset of the preceding QRS complex. This wave reaches a peak 0.19 second after its onset. Following exercise the atrial pressure rose to 36/22 mm. Hg.

The peripheral arterial saturation in this case was 91 per cent both at rest and following exercise. The cardiac index was 2.2 liters at rest, and no change occurred after exercise. A striking increase in the arteriovenous oxygen difference from 8.7 volumes per cent at rest to 12.67 volumes per cent occurred after exercise.

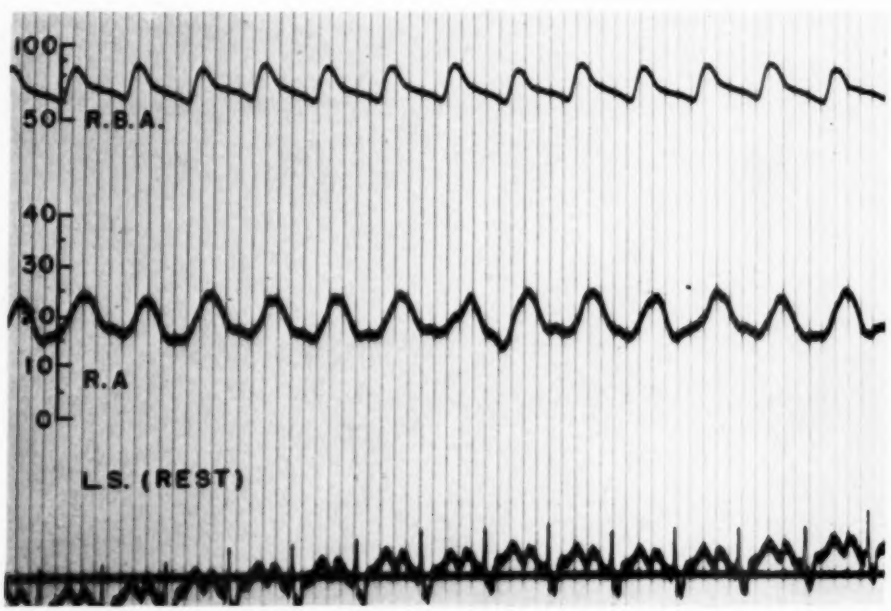


Fig. 7 (Case 3).—*A*, Right brachial artery. *B*, Right atrial pressure curve.

CASE 4.—A 49-year-old white man gave a history of cardiac decompensation five years previously. A diagnosis of rheumatic heart disease with mitral stenosis was made. Exertional dyspnea was present during the following five years. Cardiac decompensation recurred at the time of the present admission. Physical examination revealed systolic pulsations in the deep cervical veins bilaterally. The liver was moderately enlarged, and the lungs were clear. The heart was moderately enlarged both to the right and left. A systolic murmur was present at the apex and with an altered quality over the tricuspid area. A diastolic murmur was present at the apex. Atrial fibrillation, with frequent ventricular premature systoles, was present.

Physiologic Studies.—Simultaneous pressures from the right atrium and right ventricle were recorded, using a double lumen catheter (Fig. 8). The right ventricular pressure shows a systolic level of 85 mm. Hg. In early diastole the ventricular pressure falls to 9 mm. Hg and then rises to 13 mm. Hg at the end of diastole. The atrial pressure shows a rise in 0.08 second to a small peak of 15 mm. Hg in early systole. A plateau at a slightly lower pressure continues throughout the remainder of systole. At the beginning of diastole a prompt fall in pressure to levels of 9 mm. Hg occurs. Following exercise there was a slight rise in the right ventricular systolic pressure to 92 mm. Hg and a diastolic rise to 17 mm. Hg. The right atrial pressure following exercise rose to 24/12 mm. Hg. The configuration was similar to that during rest with the exception of the initial peak during systole.

The cardiac index at rest in this patient was 2.3 liters. The resting arteriovenous oxygen difference was 8.07 volumes per cent.

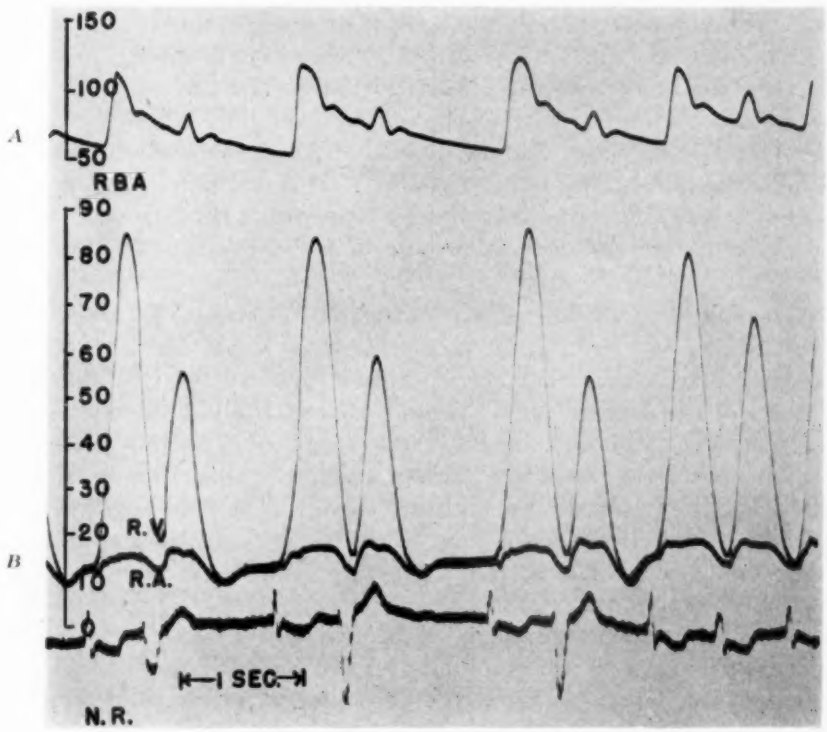


Fig. 8 (Case 4).—*A*, Right brachial artery. *B*, Simultaneous right ventricular and right atrial pressure curves.

DISCUSSION

Right Atrial Pressure Curves.—All tracings presented demonstrate that the normal systolic pressure dip, the "x" dip, is replaced by a plateau or a positive wave. This indicates the existence of tricuspid regurgitation.[7] The amplitude of this wave differs in each case and provides a basis for estimation of the severity of the tricuspid insufficiency.

The configuration of the atrial wave also varies in the four cases presented. In Case 1, there is total distortion of the normal atrial pressure curve. This effect may be termed "ventricularization" and suggests complete loss of function of the tricuspid valve. The ventricle and atrium have become essentially a common chamber. In Case 2, the resting atrial pressure wave shows evidence of

significant regurgitation. However, not until the patient exercised did the pattern of ventricularization occur. In Case 3, the aberration from the normal atrial pressure curve is less pronounced. Neither at rest nor following exercise is there evidence of free communication between the chambers of the right side of the heart. The atrial pressure curve in Case 4 shows only a minimal degree of insufficiency. The normal systolic pressure dip is replaced simply by a plateau. This type is similar to that described by Bloomfield and associates.[1]

The right atrial pressure curves in Case 1 and in Case 2, following exercise, show only minor variations from the right ventricular pressure curves. The onset of the wave occurs at the same interval following the preceding QRS complex in both atrium and ventricle, indicating a free transmission of the ventricular pressure. The time interval from the onset of the wave to the crest is considerably longer in the atrium than in the ventricle. The early diastolic dip seen in the ventricular pressure curve is not consistently present in the atrium. The atrial diastolic pressure shows a plateau identical in level and contour to that in the right ventricle. The reason for the absence of the early diastolic dip, the "y" dip, in the atrial curve is not well understood. It is suggested that the volume of blood entering the right ventricle in diastole represents a small fraction of the total volume in the atrium and great veins, and that it effects no significant pressure change.

Differentiation of Organic From Functional Tricuspid Regurgitation.—The characteristics of the right atrial pressure curves which serve to differentiate organic from functional tricuspid regurgitation have not been established. Several features of the pressure curves should be considered in attempting to make this distinction. It has been suggested that a high amplitude wave secondary to right atrial contraction indicates tricuspid stenosis, and thus establishes the presence of organic changes in the tricuspid valve.[8] The pressure waves resulting from atrial contraction in Case 3 (Fig. 7) are not increased in amplitude, and in the remaining cases atrial fibrillation was present, thus eliminating the evaluation of the atrial contraction wave as a diagnostic aid.

A second feature to be considered is the delay in the rise of the atrial pressure wave. Messer and associates,[9] employing cervical venous pulse tracing in patients with tricuspid insufficiency, suggested that a delay in the rise of the regurgitation wave was an indication of the presence of tricuspid stenosis and therefore an indication of organic tricuspid disease. A significant delay in reaching the peak of the atrial wave is seen in Cases 1, 2, and 3, while in Case 4 a summit is reached early in systole. This delay may result from obstruction of the regurgitating blood by a stenotic tricuspid valve as suggested by Messer and associates.[9] Another mechanism possibly responsible for this lag in the pressure rise is that the right atrium in organic tricuspid disease is a thin-walled distended chamber and may not register an immediate response to rise in pressure.

The presence of a "c" wave in the atrial pressure curve may indicate relatively normal motion of the tricuspid valve and thus preclude organic disease. In Case 4, and in the tracings shown by Bloomfield and associates[1] and by Richards,[2] a small well-identified pressure wave occurs very early in systole. The wave occurring at this point in normal venous pulse tracings, the "c" wave, has been attributed to the closure of the tricuspid valve leaflets.[10]

The present study suggests that the amplitude of the regurgitant wave in the atrium is the most valid basis for establishing the presence of organic tricuspid disease. The high pressure recorded in Case 1 and in Case 2 following exercise strongly indicates organic disease.

Right Ventricular Pressure Curves.—The right ventricular pressure curves in Cases 1 and 2 are characterized by notching of the systolic wave and an abrupt early diastolic dip followed by an immediate rise to an elevated plateau. The mechanism responsible for the notching is not apparent. The presence of an early diastolic dip has been described by Bloomfield and associates[1] as one of the components of the pattern of right ventricular failure.

It is proposed that the pressure level at the nadir of the early diastolic dip is a more accurate indication of the presence of failure of the right ventricle in patients with organic tricuspid regurgitation than is the plateau level in diastole. Thus, in Case 1, although a prominent early diastolic dip is present, the levels reached are still above normal and indicate right ventricular failure. In Case 2, however, the levels reached during the early diastolic dip more nearly approach normal levels and suggest a more efficient function of the right ventricular myocardium.

The pressure developed in the right ventricle (Fig. 1) by a premature ventricular contraction is seen to approximate closely the pressure developed by contractions following a longer diastolic period. This is in contrast to the wave of low amplitude seen in the peripheral arterial pulse tracing following a premature systole and presumably reflecting a similarly low pressure in the left ventricle. This development of a high systolic pressure in the right ventricle following a brief diastolic period may be due to the large residual volume of blood present in the greatly dilated right ventricle.

Comparison of the Pressure Tracings in Patients With Organic Tricuspid Disease and Constrictive Pericarditis.—In tricuspid regurgitation and in constrictive pericarditis an elevated right atrial and peripheral venous pressure is present. In both entities the elevated right atrial pressure results from a mechanical defect and does not of necessity indicate failure of the right ventricular myocardium.

It is therefore of interest to note the similarity between the ventricular pressure curves in Cases 1 and 2, and those described by Hansen and associates[11] in constrictive pericarditis. The ventricular systolic wave, in both conditions, is notched and an early diastolic dip occurs, followed by an elevated plateau during the remainder of diastole. Hansen and associates suggest that in constrictive pericarditis the high amplitude of the end-diastolic pressure does not necessarily indicate failure of the right ventricular myocardium. Thus, in both conditions, the pressure at the time of the early diastolic dip is considered the more accurate measurement of the effective function of the right ventricular myocardium.

A further similarity is seen in the presence of the low-amplitude oscillations during the period of the plateau diastolic pressure. Hansen and associates suggested that these waves result from the rapid inflow of blood from the right atrium at a high pressure, causing a water-hammer effect on contacting the ventricular wall. This same effect may possibly account for the oscillations noted in the pressure tracings in Cases 1 and 2.

SUMMARY

1. The pressure curves from the right atrium in four patients with tricuspid regurgitation are presented.

2. A pattern of severe organic tricuspid regurgitation is shown which is characterized by "ventricularization" of the right atrial pressure curve.

3. The characteristics of the pressure curves aiding in differentiating organic from functional tricuspid regurgitation are discussed.

REFERENCES

1. Bloomfield, R. A., Lauson, H. D., Cournand, A., Breed, E. S., and Richards, D. W.: Recording of Right Heart Pressures in Normal Subjects and in Patients With Chronic Pulmonary Disease and Various Types of Cardio-circulatory Disease, J. Clin. Investigation **25**:639, 1946.
2. Richards, D. W.: Observations on the Dynamics of the Systemic Circulation in Man, Bull. New York Acad. Med. **22**:630, 1946.
3. Werko, L., and Lagerlof, H.: Studies on the Circulation in Man. IV. Cardiac Output and Blood Pressure in the Right Auricle, Right Ventricle and Pulmonary Artery in Patients With Hypertensive Cardiovascular Disease, Acta med. Scandinav. **133**:427, 1949.
4. Cournand, A., and Ranges, H. A.: Catheterization of the Right Auricle in Man, Proc. Soc. Exper. Biol. & Med. **46**:462, 1941.
5. Lyons, R. H., Kennedy, J. A., and Burwell, C. S.: Measurement of Venous Pressure by Direct Method, Am. Heart J. **16**:675, 1938.
6. Val Slyke, D. D., and Neill, J. H.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and by Manometric Measurement, J. Biol. Chem. **61**:523, 1924.
7. Wiggers, C. J.: Physiology in Health and Disease, ed. 5, Philadelphia, 1949, Lea & Febiger.
8. Zeisler, E. B.: Tricuspid Stenosis, Am. Heart J. **8**:697, 1932-1933.
9. Messer, A. L., Hurst, J. W., Rappaport, M. B., and Sprague, H. B.: A Study of the Venous Pulse in Tricuspid Valve Disease, Circulation, **1**:388, 1950.
10. Hering, H. E.: Zur Analysis das Venenpulses, Deutsche med. Wchnschr. **33**:1895, 1907.
11. Hansen, A. T., Eskildsen, P., and Götzsche, H.: Pressure Curves From the Right Auricle and Right Ventricle in Chronic Constrictive Pericarditis, Circulation **3**:881, 1951.

ESOPHAGEAL PRESSURE PULSE PATTERNS (ESOPHAGEAL PIEZOCARDIOGRAM)

II. Observations in Human Beings With Mitral Valve Disease

Richard P. Lasser, M.D., Bernard Epstein, M.D., and Leo Loewe, M.D.

Brooklyn, N. Y.

THE DEVELOPMENT of corrective operations for rheumatic deformation of the mitral valve has greatly emphasized the necessity for an accurate appraisal of the nature of mitral valve lesions. Current experience has indicated that the common clinical criteria for the evaluation of mitral insufficiency or stenosis represent only a rather gross and often uncertain estimate. This is particularly true with regard to auscultatory findings, which constitute the foundation of clinical diagnosis. Murmurs with special characteristics of timing, intensity, quality, location, transmission, and pitch correlate well with the existence of specific valvular deformities in obvious cases. These same special characteristics are of limited value for the evaluation of the equivocal case. Actually, more certain diagnosis, more accurate selection of patients for operative correction, and better estimation of the prognosis of patients with mitral valve disease can be achieved by obtaining more direct information concerning the nature of the alteration of the hemodynamics within the left atrium.

The contour of the left atrial pressure pulse curve may represent a direct source of this desired information because mitral valve disease alters the normal pattern. The characteristics of the normal left atrial pressure pulse curve are well known. At the present time, little is known of the contour of the left atrial pressure curve in human beings in the presence of mitral valve disease. Our sole information is drawn from the few tracings which have been obtained directly from the left atrium during mitral valve surgery and from the patterns produced in the laboratory in experimental animals. From this admittedly limited information it has been possible to draw some tentative conclusions as to the contour of the pressure curves in mitral insufficiency, mitral stenosis, and combined lesions. The full significance of the curves is not yet understood nor has the range of variation been determined, but there is some indication that they may be of distinct diagnostic value. There is, at present, no method of recording these direct pressure pulse curves in the intact individual. Therefore, this study was undertaken to determine whether this same information could be obtained reliably by recording the pulsation in the esophagus which results from the pulsation of the left atrium. It is the graphic record of these esophageal pulsations which has been termed the esophageal piezocardiogram.

From The Jacques Loewe Research Foundation Laboratories, and the Department of Radiology, The Jewish Hospital of Brooklyn.

Aided by a grant from the Udo M. Reinach Fund.

Received for publication Aug. 8, 1952.

Anatomically, the posterior wall of the left atrium lies directly adjacent to the anterior wall of the esophagus in the region below the bifurcation of the trachea at approximately the level of vertebrae D6 and D7. Only the thin pericardium separates the two structures. At this level, moreover, no other pulsatile structure comes into contact with the esophagus since the aorta lies to the left. Contact between the aorta and the esophagus is made at a lower level, about D8. The esophagus, posteriorly, lies against a relatively rigid structure, the prevertebral muscles and vertebral column. This means that an increase in the volume of the left atrium will compress the esophagus between the expanding atrium and the vertebral column. It was previously demonstrated that the curve of esophageal pulsation, recorded with the technique described, in experimental animals, reliably mirrored the left atrial pressure pulse curve under a variety of experimental conditions.[1,2] These experimental conditions included varying degrees of mitral insufficiency, congestive failure, extrasystoles, and the infusion of pressor substances. All phases of the normal left atrial pressure curve were reproduced in the esophageal pulse curve, including the rise in pressure during atrial systole, the fall during ventricular systole (descent of the base), the pressure peak which is registered at the time of mitral valve closure, and the fall of pressure at the reopening of the mitral valve. After the production of mitral insufficiency, the esophageal pulse curve took on a characteristic contour which will be described fully later. With this experience and background, the present study of the esophageal pulse curve (esophageal piezocardiogram) in mitral valve disease in human beings was begun.

METHODS

The history of this approach, and the details of and rationale for the technique used, have been described elsewhere.[2] Briefly, the apparatus used consists of (1) a 3-foot length of polyethylene tubing with an inner diameter of 1.5 mm., (2) Sanborn electromanometer, (3) Sanborn direct-writing, multichannel electrocardiograph, and (4) heart sound microphone. The polyethylene tube is sealed at the distal end. Two small openings are made in the side of the tube about 10 cm. from the sealed end. Lead markers are placed above and below the openings; a sleeve of rubber cut from a finger of a rubber glove is drawn over the tube covering both the markers and the openings, and this is secured to the tubing with silk thread. It thus forms an inflatable sleeve in communication with the lumen of the tube. The diameter of the inflated rubber balloon is 1 to 1.5 inches. The entire system is then filled with water and all bubbles are evacuated. A three-way stopcock is fitted to the open end of the tube and this is connected to the lead tubing leading to the pressure manometer and also to a water-filled syringe. The patients who were studies were selected from the wards, clinics, and private services of The Jewish Hospital of Brooklyn. They were given 1.5 grains of Nembutal, one-half hour before the procedure, and the pharynx was anesthetized with 1 per cent Butyn Sulfate solution just prior to the introduction of the esophageal tube. The four limb leads of the electrocardiogram were attached and in some patients a heart sound microphone was strapped into place at the cardiac apex. The polyethylene tube was passed into the esophagus through the mouth

and the balloon was placed in position at the level of the left atrium under fluoroscopic control. The balloon was then inflated with 5 c.c. of water from the syringe. The tracings were taken with the patient in the erect or supine position and while he was apneic. Some tracings were obtained during deep expiration. Careful physical examination, electrocardiography, and cardiac fluoroscopy were done on each patient.

There was no interference from respiration nor waves of tonus in the esophagus because these events occur slowly; whereas, the cardiac pulsations which are recorded occur relatively rapidly in time.

There is only one serious artifact which must be avoided; if recordings are made from the lower end of the atrium, the balloon will occasionally be struck by the thoracic aorta. This results in a very sharp pressure peak in early systole. This same type of tracing can be obtained if the balloon is placed at the level of the arch of the aorta. However, if the balloon is carefully placed, a pure atrial tracing can be obtained.

There is little discomfort, the procedure generally lasts from five to ten minutes, and there have never been any ill effects.

The volume displacement of this system is very small and hence the pressure lost within the recording system is minimal. It can be readily standardized and calibrated in millimeters of mercury, and it is easy to use.

RESULTS

A. *Normal Esophageal Piezocardiogram.*—The tracings shown in Fig. 1,*A* and *B*, were selected from those which were obtained from individuals who had no evidence of heart disease. The curves though varying slightly in amplitude are all similar qualitatively. The following characteristics are discernible: (1) A rise in pressure representing atrial systole which begins 0.04 to 0.06 second after the onset of the P wave of the electrocardiogram. This pressure wave reaches a peak about 0.06 second later and then declines. (2) Next follows a series of relatively rapid oscillations which probably represent the low-frequency components of the first heart sound. Their onset, which signals the closure of the mitral valve, occurs about 0.06 second after the beginning of the QRS complex. During this period of time, the general trend of the curve is either slightly downward, or flat. The deviation from the base line, however, is slight in either case. During the remainder of the cycle, which constitutes the period of atrial filling, the curve gradually rises. The summit is reached at the time of the second heart sound, and then slightly later, at the time of the reopening of the mitral valve, there is a fall to the base line. In some tracings, these phases are less well marked than in others, but the variation is slight, and the general characteristics are the same in all.

B. *The Pathologic Esophageal Piezocardiogram.*—The tracings to be shown in this section were selected from those which were obtained from individuals with

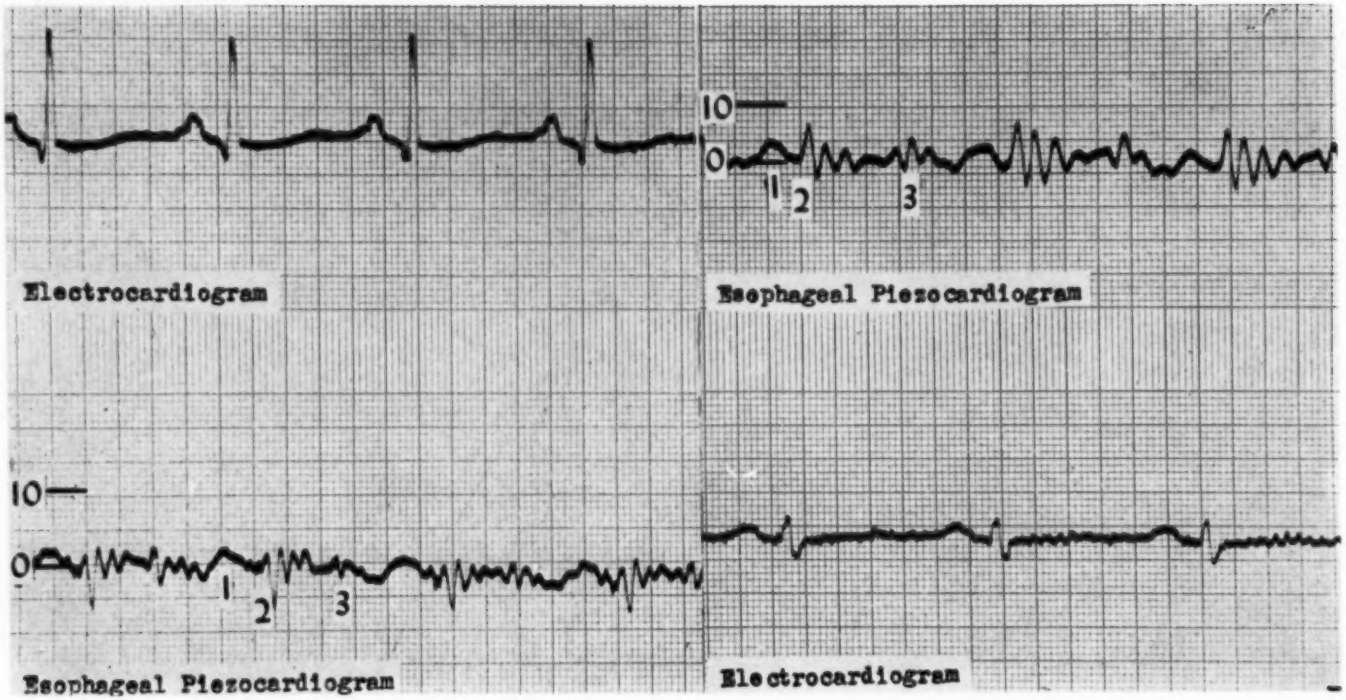
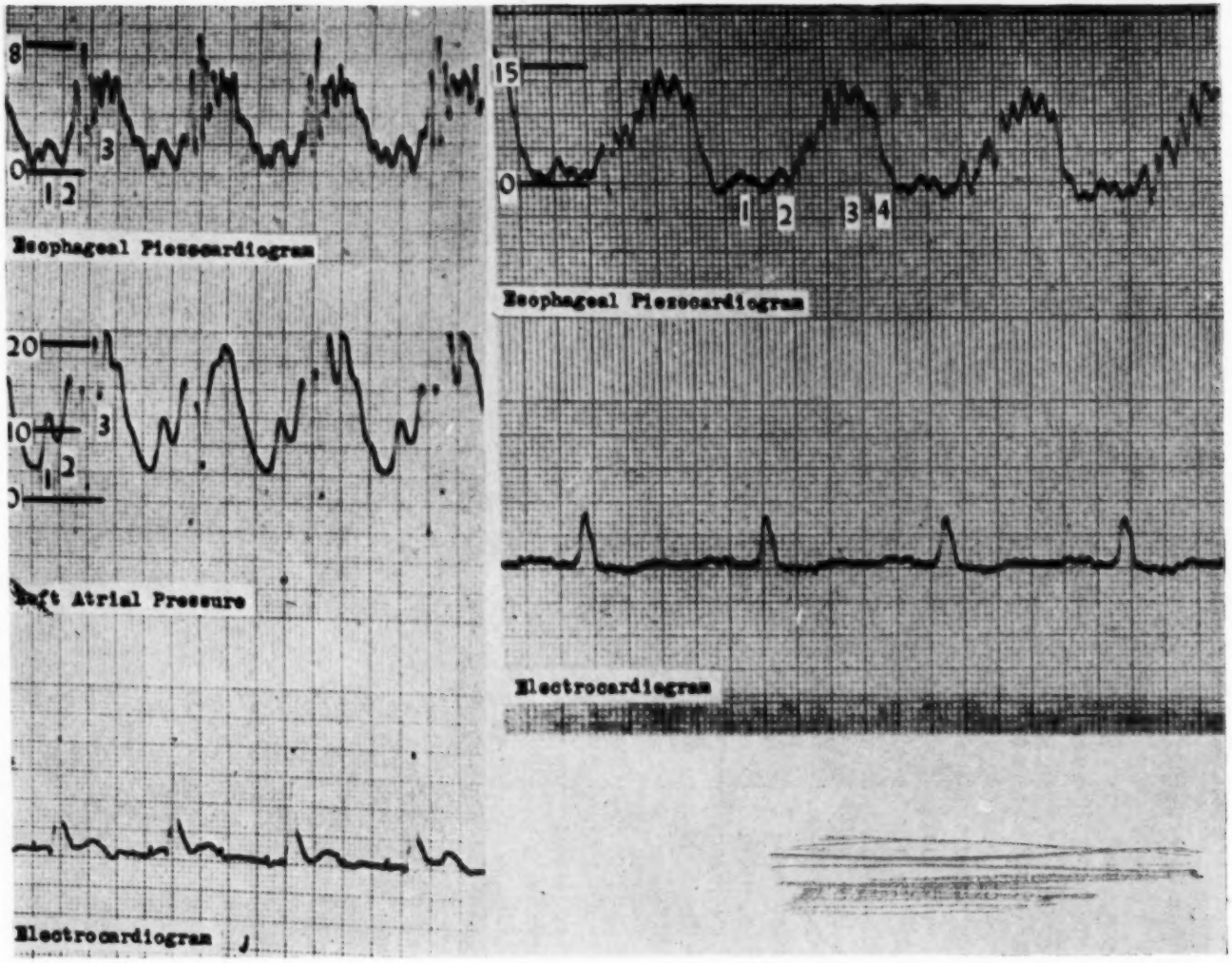


Fig. 1.—The normal esophageal piezocardiogram. *1*, Atrial systole; *2*, onset of ventricular systole; *3*, reopening of the mitral valve. Calibrations are all in mm. Hg.

well-established rheumatic heart disease. All patients were afflicted with one or more valvular lesions and several had had subacute bacterial endocarditis. Some showed minimal cardiac enlargement and were in good health while others were in advanced, chronic congestive failure. Auricular fibrillation was present in about two-thirds of the patients. In the presence of this variability, it was felt that any classification of the piezocardiograms based solely according to the clinical evaluation of the patient's valvular lesions would be inaccurate. Therefore, the piezocardiographic tracings were evaluated by comparing them with two independent standards. The first standard consisted of the large number of tracings which had been obtained in animals following the production of mitral insufficiency. The second reference source consisted of those tracings of the pressure pulses of the left atrium which had been obtained during the course of mitral valve surgery for mitral stenosis. Examples of these have been recently published by Munnell and Lam,[3] whose tracings have been reproduced here with their kind permission. It was felt that these latter tracings were a valid reference for the esophageal piezocardiograms because the experimental work in animals previously reported by us showed clearly that esophageal pulse tracings corresponded closely to simultaneously recorded pressure tracings from the interior of the left atrium. Finally, two patients of the group were subsequently operated upon and finger fracture valvuloplasty performed. In these there is as precise a knowledge of the nature of the mitral valve lesion as can be determined by finger palpation.

1. *Mitral Insufficiency.*—In Fig. 2, the esophageal pulse tracing obtained from a dog in whom experimental mitral insufficiency had been produced (*A*) is compared with a tracing obtained from a human patient with rheumatic mitral insufficiency (*B*). The great similarity between these two esophageal piezocardiograms is evident at once. Both tracings show the following characteristics: (1) A small rise of pressure (Fig. 2,*1*) which begins 0.06 second after the onset of the P wave of the electrocardiogram and is believed to represent the pressure rise of atrial systole. (2) A small pressure peak (Fig. 2,*2*) beginning 0.06 second after the onset of the QRS complex. This peak is believed to result from mitral valve closure. (3) A marked rise of pressure which reaches a peak (Fig. 2,*3*) just prior to the reopening of the mitral valve. This rise in pressure during the period of ventricular systole is the result of the regurgitation of blood from the ventricle into the atrium through the incompetent mitral valve. This results in an increase in both the atrial pressure and volume. Note that a great increase in pressure does not take place at once in the earliest phase of ventricular systole. The pressure increases gradually in magnitude and reaches a maximum just prior to reopening of the mitral valve. (4) Finally, a precipitous fall in pressure is seen following the reopening of the mitral valve.

The patient from whom this tracing was obtained was a 39-year-old woman with a history of acute rheumatic fever at the ages of 6 and 11 years. She was in congestive failure and was severely dyspneic and orthopneic. Her heart was enlarged, and an apical, systolic thrill was palpable. The first heart sound was replaced by a murmur which continued throughout systole. The murmur was of Grade IV intensity and was harsh and widely transmitted. Fluoroscopic observations revealed that the left atrium was moderately enlarged; there was a moderate degree of left ventricular enlargement and some increase in the size of the right ventricle and right atrium.



A *B*

Fig. 2.—The esophageal piezocardiogram in mitral insufficiency. *A*, Experimental tracings obtained from the esophagus and left atrium simultaneously in a dog. *B*, Tracing obtained from a human being. *1*, Atrial systole; *2*, onset of ventricular systole; *3*, late systolic pressure peak of mitral insufficiency; *4*, fall in pressure following reopening of the mitral valve. Note the marked rise in pressure during ventricular systole, between *2* and *3*, which results from mitral regurgitation.

Comment.—These tracings demonstrate the great resemblance between the piezocardiograms obtained in experimental animals after the production of mitral insufficiency, and those obtained from human beings with rheumatic mitral insufficiency. The noteworthy feature is the presence of a positive pressure wave of considerable size during ventricular systole. This is in contrast to the normal tracings where this part of the curve is either flat or shows only a very slight positive deviation. This rise of atrial pressure which is created by regurgitation of blood from the ventricle into the atrium is related to the magnitude of regurgitation. The magnitude of regurgitation, in turn, is related to the extent of the incompetence of the mitral valve. However, it would probably be difficult to estimate accurately the magnitude of regurgitation by merely measuring the height of this peak. The exact relationship between the height of the pressure peak and the magnitude of regurgitation is modified by such factors as the pressure-volume characteristics of the atrial wall, the duration of the isometric contraction phase of ventricular systole, the height of the pressure generated within the left ventricle during systole, the cardiac output,[4] etc.

The positive pressure wave which appears in the atrium as a result of mitral regurgitation has a characteristic form. It has been pointed out by Wiggers[4,5] and has been confirmed by our own observations that the atrial pressure does not rise markedly during the isometric contraction phase of ventricular systole. There is a progressive rise in pressure which reaches a maximum after the systolic pressure rise in the ventricle has begun to decline. Thus the atrial curve shows a late systolic pressure peak. A similar wave form has been observed by Gorlin and associates[6] in their study of the "pulmonary capillary pressure" in mitral insufficiency.

These pulmonary capillary pressure tracings presumably represent the retrograde transmission of the pressure pulses of the left atrium through the pulmonary venous system. This same wave form has been noted in direct left atrial tracings in human beings.[3] In view of these findings, this wave form which appears in the esophageal piezocardiograms is believed to be characteristic of mitral insufficiency.

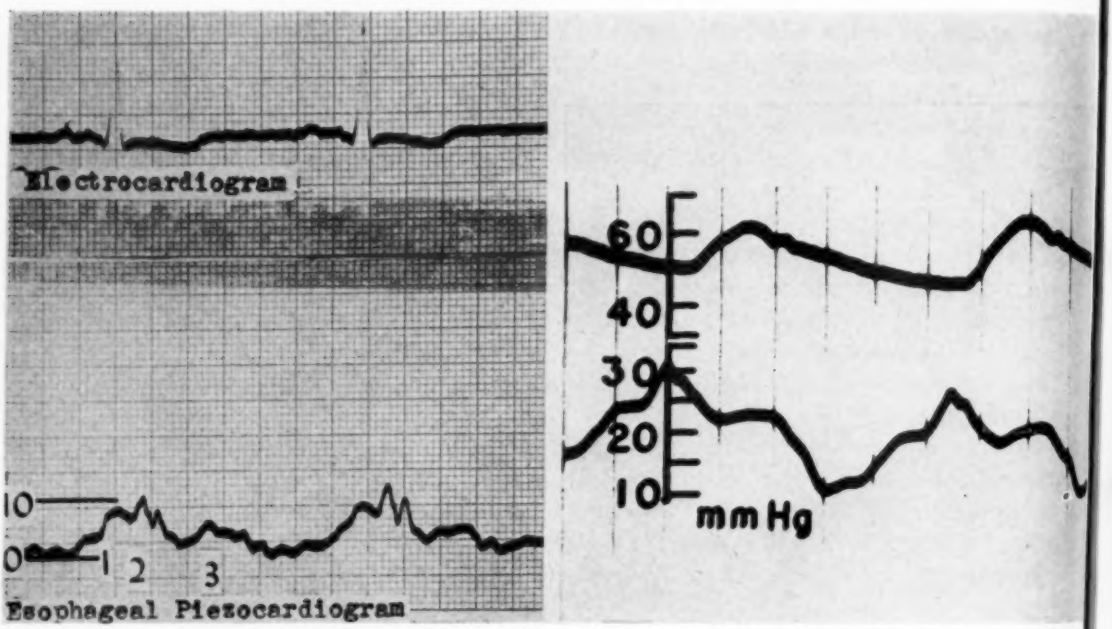
2. *Mitral Stenosis.*—The piezocardiograms shown in Figs. 3,*A*, and 4,*A*, are believed to be characteristic of severe mitral stenosis without a significant degree of mitral insufficiency. This belief is founded in part upon the resemblance between these wave forms and those pressure tracings obtained by Munnell and Lam[3] from the chamber of the left atrium during the progress of operations for relief of mitral stenosis. These direct atrial pressure tracings are reproduced in Figs. 3,*B*, and 4,*B*. Confirmatory evidence of the nature of the mitral valvular lesion was secured by digital palpation in the case of Fig. 3,*A*, at the time of mitral valve surgery. Additional corroborative evidence accrued from the results of a post-mortem examination which was performed six weeks after the tracings shown in Fig. 4,*A*, were obtained.

Fig. 2.—The esophageal piezocardiogram in mitral insufficiency. *A*, Experimental tracings obtained from the esophagus and left atrium simultaneously in a dog. *B*, Tracing obtained from a human being. *1*, Atrial systole; *2*, onset of ventricular systole; *3*, late systolic pressure peaks of mitral insufficiency; *4*, fall in pressure following reopening of the mitral valve.

Both the direct atrial tracing in Fig. 3,*B*, and the esophageal piezocardiograms in Fig. 3,*A*, have the following characteristics: (1) A rise in pressure attributable to atrial systole. (2) A sharp peak beginning 0.06 second after the onset of the QRS complex, marking the time of mitral valve closure. (3) During

the remainder of ventricular systole there is a fall in pressure followed by a small rounded wave of low amplitude.

The tracings shown in Fig. 4, *A* and *B*, show a somewhat different wave form from those in Fig. 3, although both were obtained from patients with presumably isolated mitral stenosis. The esophageal curve and the direct atrial curve in Fig. 4 show the following characteristics: (1) A pressure peak accompanying atrial contraction which may or may not be present depending on whether sinus rhythm or auricular fibrillation is present. (2) A prompt, steep elevation of intra-atrial pressure occurring 0.06 to 0.08 second after the beginning of the QRS complex (Fig. 4,*2*). This sharp upstroke which probably begins with mitral valve closure attains the maximum pressure recorded by the curve. Thus the



A *B*

Fig. 3.—Isolated mitral stenosis. *A*, Esophageal piezocardiogram. *B*, Direct left atrial pressure tracing. (From Munnell, E. R., and Lam, C. R., Cardiodynamic Effects of Mitral Commissurotomy. Circulation 4:321, 1951.)

Note the rise of pressure with atrial systole (*1*), pressure peak of mitral valve closure (*2*), and small rounded wave of low amplitude (*3*).

pressure maximum is reached in the early phase of ventricular systole and not in the late phase of systole as is the case with mitral insufficiency. This distinguishing characteristic is of considerable interest. Why the atrial pressure should rise so abruptly in mitral stenosis is difficult to answer. It is possible that the great residual pressure and blood volume within the pulmonary system fills the atrium to capacity just as soon as the mitral valve closes. (3) There may be a slight to moderate decline in the pressure seen during the next portion of the curve (Fig. 4,*3*). (4) The pressure returns approximately to the previous maximum level and remains at this level, forming a plateau for the remainder of ventricular systole (Fig. 4,*4*). (5) With the reopening of the mitral valve, the pressure falls, somewhat more gradually than in the tracings of patients with mitral insufficiency.

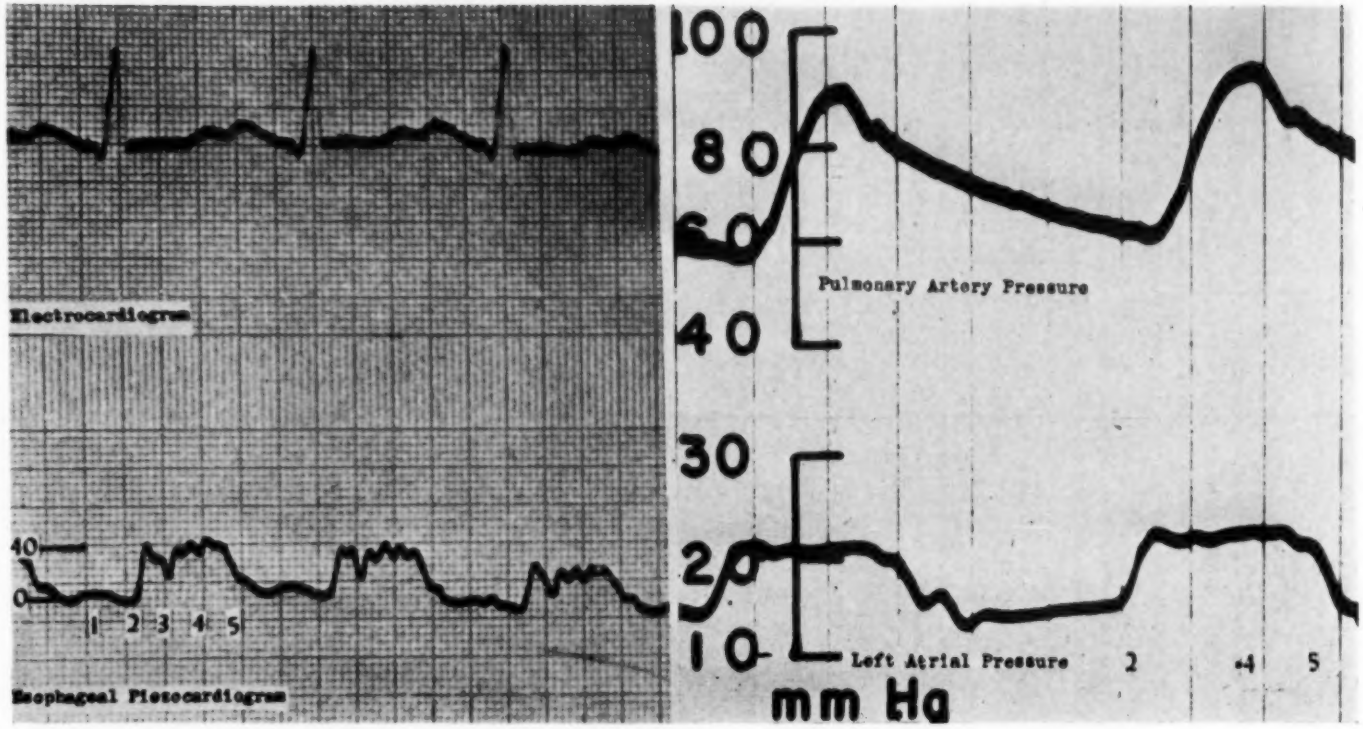
The patient whose tracings are shown in Fig. 3, *A*, was a 26-year-old woman who was becoming increasingly incapacitated by dyspnea and fatigue. The heart was not grossly enlarged; a rumbling diastolic murmur and mitral click were audible. Cardiac fluoroscopy revealed the presence of left atrial, pulmonary artery, and right ventricular enlargement and the absence of left ventricular enlargement. A finger fracture commissurotomy was performed, at which time the presence of a severe degree of isolated mitral stenosis without insufficiency was found.

The patient in Fig. 4, *A*, was a 31-year-old man who had had acute rheumatic fever at the age of 7 years, was treated and cured of subacute bacterial endocarditis 5 years previously, and was currently in congestive failure with marked dyspnea and orthopnea. A Grade II late systolic murmur was heard at the apex as well as a diastolic and presystolic murmur in the same location. A mitral click was audible. A soft, blowing, diastolic murmur was heard along the left sternal border. The electrocardiogram showed sinus rhythm, large P waves, and a marked right ventricular hypertrophy pattern. Fluoroscopy showed considerable enlargement of the left atrium, right ventricle, right atrium and pulmonary artery, and possibly slight enlargement of the left ventricle. Calcification of mitral valve leaflets was noted. He expired suddenly after minimal exertion. At post mortem his heart was enlarged and most of the enlargement was due to a hypertrophied and dilated right ventricle. The left atrium was also dilated and hypertrophied. The mitral valve was calcified and markedly stenotic. The orifice was in the form of a fish mouth whose widest diameter was about 0.5 to 0.75 cm. The borders of the orifice were not rigid, but were plastic and seemed to be capable of close apposition. The left ventricular wall was of normal thickness and the chamber was not dilated. Thus the anatomic lesion consisted of a marked degree of mitral stenosis with a very minimal, if any, degree of mitral insufficiency.

Comment.—In this section we have presented tracings which we believe to be characteristic of mitral stenosis, and have cited the evidence upon which this conclusion is based. It is possible that there may be several other wave forms which may be found in pure mitral stenosis.

However, there is no difficulty in distinguishing these wave forms from those described in mitral insufficiency. It is felt tentatively that the important diagnostic consideration consists of the absence of any pronounced late systolic secondary pressure peak such as characterizes mitral insufficiency.

3. *Mitral Stenosis With Insufficiency.*—The most commonly encountered form of rheumatic mitral valve disease is a combination of both stenosis and insufficiency. However, in a certain number of patients whose predominant lesion is one of mitral insufficiency, it is clinically difficult to ascertain the presence of this lesion. Consequently some of these patients have been explored for the purpose of performing a commissurotomy and at operation have proved to be unsuitable by virtue of marked regurgitation. The atrial and esophageal pressure pulse patterns may offer much assistance in this regard. In this section, tracings will be presented which are believed to show evidence of both lesions. The tracing in Fig. 5 was obtained preoperatively from a patient who was subsequently subjected to a finger fracture valvuloplasty. At operation, a very marked mitral stenosis was found. The valve orifice did not admit the tip of the index finger. In addition, a small amount of regurgitation was encountered. The procedure was completed without increasing the extent of regurgitation. The tracings show a rise in pressure attributable to atrial systole, a sharp early systolic peak followed by a slight secondary rise in pressure, and a late secondary peak which is higher than the primary peak. Since we know that this patient did show evidence of some slight regurgitation we can compare this wave contour with the tracings shown in the previous section and, by the difference between them, possibly



A *B*

Fig. 4.—Isolated mitral stenosis. *A*, Esophageal piezocardiogram. *B*, Direct left atrial pressure tracing. (From Munnell and Lam, Circulation, 1951.)

1, Atrial systole; *2*, early systolic pressure peak at onset of ventricular systole; *3*, slight fall in pressure; *4*, systolic plateau; *5*, fall in pressure following reopening of the mitral valve.

Note the characteristic early systolic pressure peak and systolic plateau in both tracings similarly.

establish the effect of minimal regurgitation upon the contour of the curve. This curve most closely resembles that of Fig. 4,*A*. A difference between the two is observed during the last half of the period of ventricular systole. Whereas this portion of the curve is a plateau in the tracing of isolated mitral stenosis, the tracing here shows a secondary rise and a small late secondary peak. It is this secondary pressure peak which is tentatively considered to be evidence of mitral insufficiency in the presence of mitral stenosis.

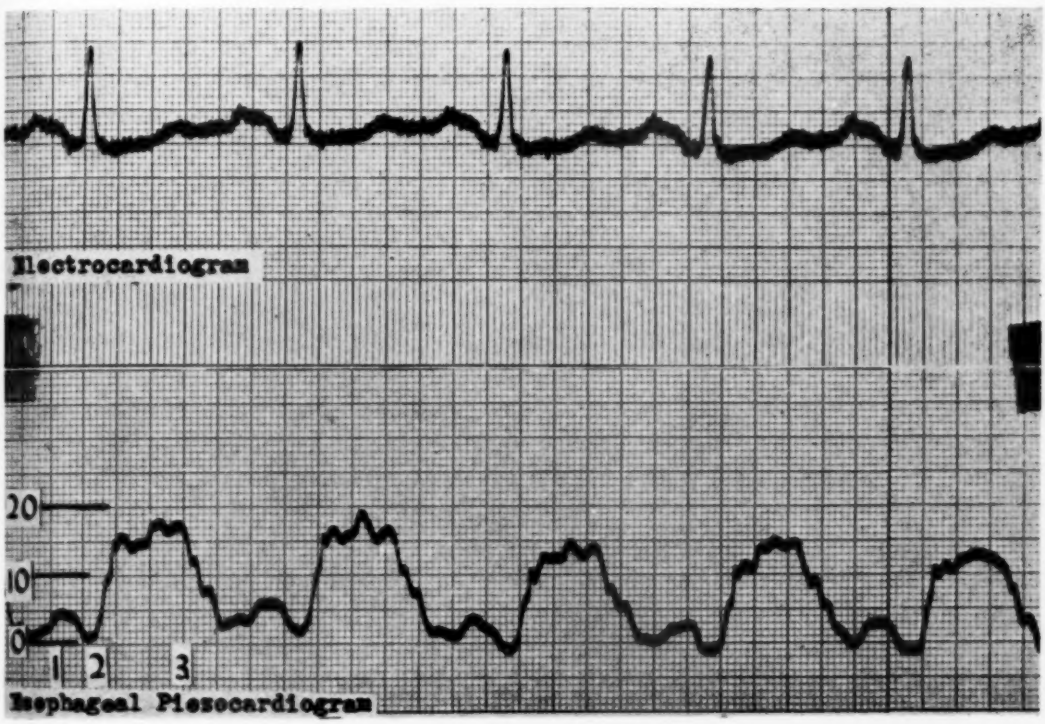
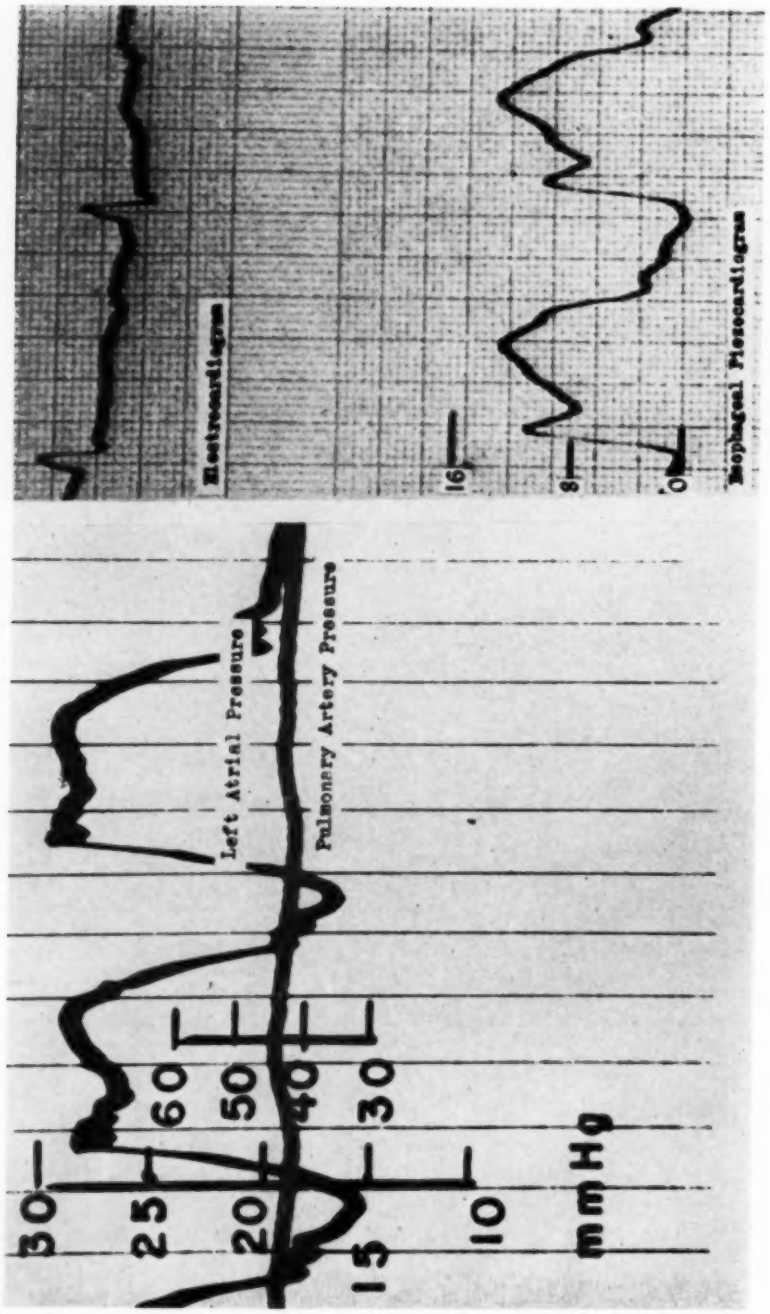


Fig. 5.—Mitral stenosis with minimal insufficiency (esophageal piezocardiogram). *1*, Atrial systole; *2*, early systolic pressure peak at onset of ventricular systole; *3*, secondary late systolic pressure peak.

Note that the difference between this tracing and that of Fig. 4 consists in the superimposition of a secondary late systolic pressure peak. This is believed to indicate the presence of regurgitation.

Comment.—To illustrate again the close parallel between these esophageal piezocardiographic tracings and direct intra-atrial pressure tracings, we reproduce Fig. 6,*A*, (a tracing published by Munnell and Lam). In their publication, they stated that this patient had both insufficiency and stenosis as determined by finger palpation.[3] In Fig. 6,*B*, is shown an esophageal piezocardiogram from a patient who clinically showed obvious evidence of both mitral stenosis and insufficiency. The close resemblance between these two tracings is obvious. The characteristics described for the piezocardiographic tracings in Fig. 5 are clearly seen in both of these tracings. We note the sharp, early systolic pressure peak, the secondary rise, and the secondary late systolic peak. It is to be noted that



A B

Fig. 6.—Mitral stenosis with substantial insufficiency. *A*, Esophageal piezocardiogram. *B*, Direct left atrial pressure tracing. (From Munnell and Lam, Circulation, 1951.)
Note the early systolic pressure peak, the pronounced secondary rise in pressure, and marked late systolic pressure peak.

the secondary, late systolic pressure peak is more pronounced in these tracings in Fig. 6 than in those of Fig. 5. It is believed that this may indicate a greater degree of mitral insufficiency.

SUMMARY

It would appear from this study that one can determine the contour of the left atrial pressure pulse curve by recording esophageal pulsations at the level of the left atrium with the technique which has been described. This relationship between the intra-atrial pressure pulse contour and the contour of the esophageal pressure pulse tracing (piezocardiogram) has been demonstrated by two kinds of evidence. The first evidence consisted of a study in animals wherein simultaneous recordings were made of left atrial pressure curves and curves of esophageal pressure pulsations. These studies showed that all phases of the atrial pressure curve were transmitted to the esophageal curve. The second type of evidence consisted in a comparison between direct intra-atrial pressure tracings which had been obtained by other investigators in human beings with mitral valve disease and the esophageal piezocardiograms which had been obtained by us in other human beings who also had mitral valve disease. This evidence, though circumstantial in a sense, appeared to us to be strongly convincing. Absolutely conclusive proof in human beings of the identity between the two sets of curves could be obtained only by simultaneous recording of the direct atrial and esophageal pressure curves in the same individual during mitral valve surgery. We have not yet been able to accomplish this.

On the basis of the comparative evidence discussed above, it was possible to tentatively divide the piezocardiographic tracings into three categories, namely, predominant mitral insufficiency, mitral stenosis without insufficiency, and mitral stenosis with insufficiency.

Tracings of patients with mitral insufficiency were characterized by a positive pressure wave which began its ascent in ventricular systole, rose progressively, and reached a peak in late systole just prior to the opening of the mitral valve. The pressure then declined precipitously. This wave contour corresponded very closely to the findings of Wiggers[4,5] in animals with experimentally induced mitral insufficiency. He emphasized that the increase in atrial pressure and volume due to regurgitation did not reach substantial proportions in the early phases of ventricular systole. The greatest amount of regurgitation occurred during the latter phases of ventricular ejection, increasing even as ventricular pressure began to fall.

The tracings of patients who had mitral stenosis with no insufficiency were characterized by a sharp, early systolic pressure peak and either a plateaulike sustained pressure elevation during the remainder of ventricular systole or a fall in pressure followed by a rounded wave of low amplitude.

The tracings of patients with combined mitral stenosis and insufficiency were characterized by an early systolic pressure peak followed by a secondary rise in pressure beginning in mid-systole which then formed a secondary pressure peak in late systole. This secondary peak was often higher than the primary peak.

Though we have shown that the contours of the esophageal and intra-atrial pressure curves are very similar, we do not wish to imply that one can determine the actual level of pressure within the atrium with this technique.

Other techniques which have been applied to the study of mitral valve disease, such as cardiac catheterization,[6,7,8] particularly the recording of the pulmonary capillary pressure,[9,10] and electrokymography,[11] supply vital information about cardiopulmonary dynamics. However, none of these yields the type of information about the contour and range of variation of the left atrial pressure pulsation that this technique of esophageal recording does. We feel, therefore, that it offers useful, direct information about the nature of the impairment of the mitral valve.

CONCLUSIONS

Pulsations in the esophagus at the level of the left atrium have been recorded and studied in normal individuals and in those with mitral valve disease. Recordings were made by means of a small balloon attached to a polyethylene esophageal tube. Previous studies in animals had demonstrated that the contour of the esophageal pulse curve, recorded with the described technique, closely paralleled that of the pressure pulse curve obtained simultaneously from the interior of the left atrium. These observations included experimentally induced mitral insufficiency, mitral stenosis, and congestive failure.

It was possible to arrive at a classification and interpretation of the esophageal pressure curve in human beings by extension of the experimental observations and by comparing esophageal piezocardiograms with published tracings obtained by other investigators directly from the left atrium in human beings with mitral valve disease.

1. Distinctive patterns were found to characterize individuals with no heart disease, those with mitral insufficiency, those with mitral stenosis without insufficiency, and those with combined mitral stenosis and insufficiency.

2. The term esophageal piezocardiogram has been proposed to describe this type of recording in order to describe its nature and to distinguish it clearly from the esophageal electrocardiogram.

3. It is suggested that the esophageal piezocardiogram supplies valuable information about the presence or absence of mitral valve disease and may make possible a reliable estimation of the nature of mitral valve lesions.

We wish to express our appreciation to Mr. Paul Geller and Mrs. Selma Rachlin for their technical assistance.

REFERENCES

1. Lasser, R. P., and Loewe, L.: Characteristic Pressure Pulses Recorded With an Esophageal Balloon in Experimental Mitral Insufficiency in Dogs, Proc. Soc. Exper. Biol. & Med. **77**:798, 1951.
2. Lasser, R. P., and Loewe, L.: Esophageal Pressure Pulse Patterns (Esophageal Piezocardiogram). I. Experimental Observations, Am. Heart J. **44**:531, 1952.

3. Munnell, E. R., and Lam, C. R.: Cardiodynamic Effects of Mitral Commissurotomy, Circulation **4**:321, 1951.
4. Wiggers, C. J.: Modern Aspects of Circulation in Health and Disease, Philadelphia, 1923, Lea & Febiger.
5. Wiggers, C. J., and Feil, H.: Circulatory Dynamics in Mitral Insufficiency, Heart **9**:149, 1922.
6. Gorlin, R., Haynes, F. W., Goodale, W. T., Sawyer, C. G., Dow, J. W., and Dexter, L.: Studies of the Circulatory Dynamics in Mitral Stenosis: Altered Dynamics at Rest, Am. Heart J. **41**:30, 1951.
7. Bloomfield, R. A., Lawson, H. D., Cournand, A., Breed, E. S., and Richards, D. W., Jr.: Recording of Right Heart Pressure in Normal Subjects and in Patients With Chronic Pulmonary Disease and Various Types of Cardiocirculatory Disease, J. Clin. Investigation **25**:639, 1946.
8. Hickam, J. B., and Cargill, W. H.: Effect of Exercise on Cardiac Output and Pulmonary Arterial Pressure in Normal Persons and in Patients With Cardiovascular Disease and Pulmonary Emphysema, J. Clin. Investigation **27**:10, 1948.
9. Hellems, H. K., Haynes, F. W., and Dexter, L.: Pulmonary "Capillary" Pressure in Man, J. Appl. Physiol. **2**:24, 1949.
10. Eliasch, H., Wade, G., and Werko, L.: The Effects of Work on the Pulmonary Circulation in Mitral Stenosis, Circulation **5**:271, 1952.
11. Luisada, A. A., and Fleischner, F. G.: Dynamics of the Left Auricle in Mitral Valve Lesions: Fluorocardiographic Study, Am. J. Med. **4**:791, 1948.

ELECTROCARDIOGRAPHIC ASSESSMENT OF POSTERIOR CARDIAC INFARCTION

CORNELIO PAPP, M.D., AND K. SHIRLEY SMITH, M.D., F.R.C.P.

LONDON, ENGLAND

COMPARISON between clinical symptoms and electrocardiographic signs in cardiac infarction led to the recognition of a group of patients with slight cardiac infarction. In these, cardiac pain, more often prolonged but sometimes of the type of angina of effort, was the main clinical feature, while shock, cardiac failure, laboratory and clinical signs of tissue destruction were absent.[1] The electrocardiographic signs were characteristic inasmuch as changes in S-T and T pattern were constant features and these were only rarely associated with pathologic Q waves and abnormal ventricular complexes.[2] Clinical recovery in almost all and electrocardiographic recovery in many of these patients justified the designation "slight." Recent necropsy control in two patients showed that these cardiographic changes corresponded to small areas of infarction and represented the acute stage of patchy myocardial sclerosis. These changes were not due to local arterial occlusion but to arteriosclerotic narrowing of the main coronary arteries.

In a consecutive series of 128 cases of anterior and anterolateral cardiac infarction, fifty-four (42.2 per cent) were classified as slight while in a consecutive series of seventy-two posterior, posterolateral, and posteroanterior infarctions only sixteen (22.2 per cent) were of this type. This confirmed our first impression, of a limited series of thirty-five slight infarctions of which only nine (25.7 per cent) were of posterior type, that slight posterior infarction is much less common than slight anterior cardiac infarction.

In the diagnosis of slight posterior infarction there are special diagnostic difficulties and this circumstance may have resulted in misleading figures through failure to establish the diagnosis in a number of cases. In addition to the diagnostic problems encountered in posterior infarctions in general due to positional variations of the heart, the frequent absence of Q waves or their late and temporary appearance makes the electrocardiographic diagnosis even more difficult in these slight cases. The presence of R-T and T changes in Leads II, III, and aV_F without pathologic Q waves may be inconclusive evidence though it perhaps ". . . indicates that the infarct is relatively superficial."[3] In small posterior infarcts confined to the apical or basal one-third of the posterior ventricular wall, Lead aV_F may not be diagnostic[4] and "pure" posterior infarcts may escape electrocardiographic detection altogether except by esophageal leads,[5] particularly if the location is high, near the auricular margin.[6] Esophageal leads, on the

From the Cardiac Department, Charing Cross Hospital, London, W.C.2.
Received for publication July 17, 1952.

other hand, were not more helpful in Bain's experience,[7] and Oram, Holt, and East[8] consider aV_F leads even superior. Before Lead aV_F came into general use, Rosenbaum, Wilson and Johnston[9] suggested additional unipolar leads from the back; later Sears and Myers[10] recorded nine leads at three levels from V_7 to V_9, and concluded that these were helpful in estimating the extent of infarction though they failed to reveal definite infarcts in a few where esophageal leads were conclusive. Slapak and Partilla[11,12] reverted to bipolar leads and modified Nehb's[13] leads; they fixed the electrode of the left arm in C_7 position and, by displacing the right arm electrode from the left sternal border to the anterior axillary line in the second space along a horizontal line, they took three records in positions C_2, C_4, and C_6 with the switch on Lead I. They claim that these leads are superior to Leads III and aV_F. Evans[14] believed he had overcome all diagnostic difficulties with Lead III R—Lead III recorded in deep inspiration. In a number of his patients, lowering of S-T and T in Lead III R provided the only cardiographic abnormality in patients with previous or subsequent infarctions which, however, were not always posterior.

With these controversies in mind, we have sought to establish the diagnosis of slight posterior cardiac infarction and to find out its incidence in posterior cardiac infarction in general. In view of the unfavorable reports on esophageal leads and their inherent difficulties, these were not used. In doubtful cases, the usual twelve-lead record was supplemented by III R and aV_{FR}, and the new leads proposed by Slapak and Partilla were tried. A new approach was made to the problem by subjecting the patients to effort tests. We were careful thereby to avoid any rigid standards and were guided exclusively by the patient's effort tolerance. When effort tolerance was good the patient mounted at a quick pace one or two flights of stairs;[15] when it was poor Master's steps were used[16] till the patient complained of slight sternal discomfort. All these patients were ambulant and the effort they performed during the test was not more than that which they had repeatedly undertaken during their daily routine. It was also hoped that by comparing clinical and electrocardiographic signs in a large series of cases of posterior infarction the prognostic significance of some of the grave signs of posterior infarction, such as septal extension, heart block, and arrhythmias, could be better assessed.

MATERIAL AND METHOD OF INVESTIGATION

One hundred consecutive cases of acute posterior cardiac infarction were assessed according to the severity of the clinical symptoms during the attack and classified, following the principles set out in previous papers,[1,2] into slight, moderate, and severe. Cases from previous series were included where the exact date of infarction was known or could be approximately determined. Patients with repeated posterior cardiac infarctions were assessed for the last one. The electrocardiograms were arbitrarily divided, according to the R-T-T changes they exhibited, into three groups. Those with R-T elevation and monophasic T waves were classified as "acute"; those with bowing of the R-T period and deep T inversion as "subacute"; and those with R-T segment at a level, with

pathologic Q waves and flat T inversion in Leads II, III, and aV_F, as "chronic." When there were diagnostic difficulties the routine twelve-lead record was supplemented by further leads and the patient was subjected to an effort test. The electrocardiographic changes found were correlated with the time which elapsed since the infarction; the presence or absence of pathologic Q waves was noted; attention was also directed to reciprocal changes (R-T depression in anterior chest leads in conjunction with tall T waves) and to patterns representing lateral or septal extension. While frequent records were taken during the two months' period of close observation, the first record was compared with the one recorded at the end of this period and classified as restored, improved, unchanged, or worse. The record was considered "improved" when it changed grouping, for example, when the acute changes became subacute or the subacute changes chronic. It was considered "worse" when new areas became involved, though the areas of original infarction may have shown regressive changes.

GENERAL DATA

The age and sex table (Table I) shows the well-known facts that the main incidence of cardiac infarction between the ages of 50 to 70 years and the almost fivefold preponderance of men over women is equally applicable to posterior cardiac infarction. It justifies this investigation, for the incidence of slight posterior infarction is 22 per cent, as against 42 per cent of slight cases in anterior cardiac infarction. In posterior infarction, the incidence of the severe ones is 57 per cent, as against 35 per cent in anterior infarction (Table II). This shift toward gravity is partly due to the fact that three patients (Cases 68, 74, 85) who had slight posterior infarctions during the two months of close observation developed severe cardiac infarctions, a behavior hardly observed among fifty-four patients with slight anterior infarctions. They were listed as severe cases. Another reason is the well-known preponderance of arrhythmias and complete heart block in posterior cardiac infarction, mainly responsible for the severe shock in cardiac infarction without pain.[17] The incidence of the moderate cases was found fairly equal—21 per cent in posterior as against 22.6 per cent in anterior cardiac infarction.

TABLE I. AGE AND SEX IN 100 PATIENTS WITH POSTERIOR CARDIAC INFARCTION

GRADING OF POSTERIOR INFARCTION	40 TO 49 YRS.		50 TO 59 YRS.		60 TO 69 YRS.		70 YRS. AND OVER		TOTAL
	M	F	M	F	M	F	M	F	
Slight	5	–	6	1	5	4	1	–	22
Moderate	2	–	7	–	6	3	3	–	21
Severe	7	1	17	4	17	3	6	2	57

Proportion of men to women, 4.6:1.

TABLE II. ELECTROCARDIOGRAPHIC PATTERN IN 100 CASES OF POSTERIOR CARDIAC INFARCTION

PATTERN	22% SLIGHT (42%A)*	21% MODERATE (23%A)*	57% SEVERE (35%A)*
Acute	1	9	43
Subacute	19	12	14
Chronic	2	—	—
No. Q waves	12	3	2†
Lateral extension	9	15	30
Posteroanterior infarction	—	1	18
Heart block	—	—	14
Arrhythmias	—	—	10
Electrocardiogram restored	5	—	—
Electrocardiogram improved	9	11	25
Electrocardiogram unchanged	5	9	18
Electrocardiogram worse	3	1	11‡
Patient recovered	22	21	38
Patient died	—	—	19

*Incidence in 150 consecutive cases of anterior (A) infarction.
†One bundle branch block, one early recording.
‡Three died before second recording.

ELECTROCARDIOGRAPHIC PATTERNS IN SLIGHT, MODERATE, AND SEVERE POSTERIOR CARDIAC INFARCTION (TABLE II)

1. *Acute Pattern.*—This was exceptional in slight posterior cardiac infarction, more common in moderate cardiac infarction and almost the rule in severe posterior infarction shown by about three-fourths of these patients. Though the rarity of the acute changes in slight cardiac infarction may have been due to the time which elapsed between the attack and the first electrocardiogram, it was remarkable that in the six patients recorded within days it was seen only once. In the severe group with dramatic symptoms and in which electrocardiograms were recorded within days, and often on the day of the attack, thirty-eight out of forty-two patients showed an acute pattern and four showed a subacute one. Yet, an acute pattern was seen in five further patients recorded twelve, fifteen, twenty-five, thirty-four, and fifty days after the attack. Since severe cardiac infarction means extensive tissue destruction, this finding is consistent with the electrocardiographic signs described in ventricular aneurysm in which acute changes tend to persist indefinitely.[18] The subacute changes, bowing of the R-T segment and deep T inversion, were seen as early as the day following the attack and as late as one month after the attack in the slight cases. In the moderate and severe ones, they often formed a persistent pattern.[19] Their proportion was greatest in the slight cases and smallest in the severe ones. Only two patients, and they belonged to the slight group, were found with "scar" pattern and, in both, the record was taken weeks after the approximate date of infarction.

2. *Absence of Q Waves.*—More than one-half of the slight cases did not show any pathologic Q waves in the first electrocardiogram, though in six of these they appeared later, sometimes as late as two months after infarction (Fig. 10). One of the main diagnostic difficulties was the distinction of the QS of the horizontal

heart in Lead III from a pathologic Q^{20} though a borderline Q in Lead II and the corresponding R-T changes in Leads II and III were often characteristic (Fig. 1). In later records of Case 14, QR in Lead III developed and this was carried to a smaller extent into aV_F. The patient died three and one-half years after the slight

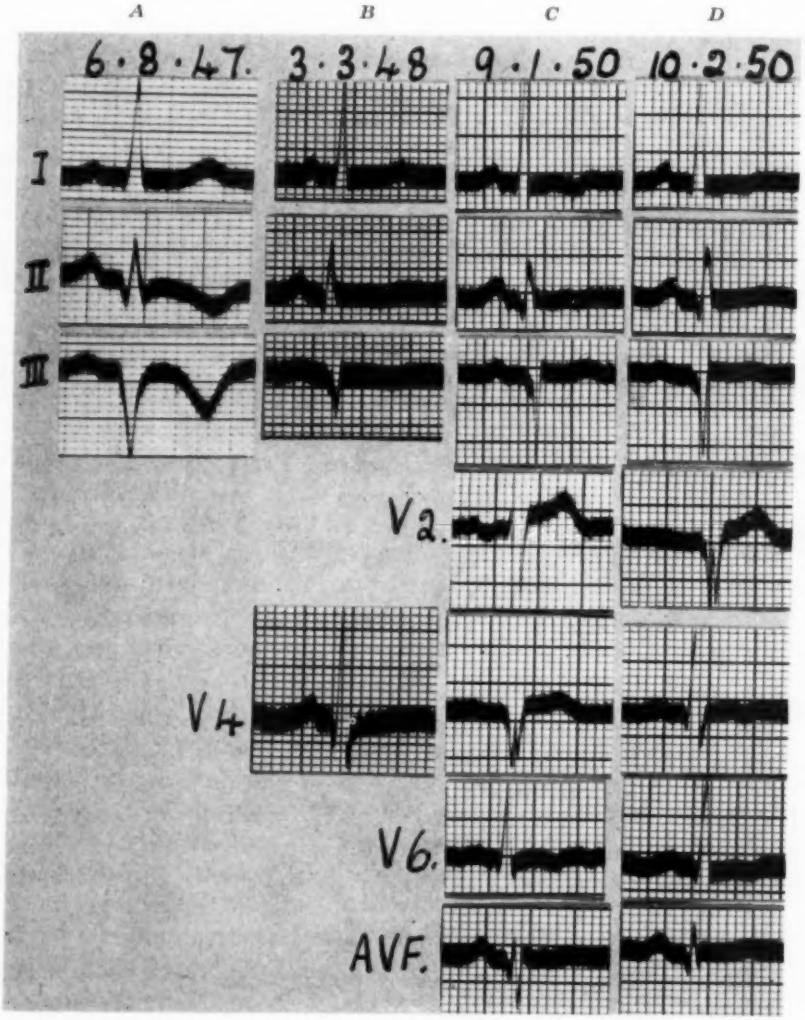


Fig. 1 (Case 14).—Electrocardiogram of a 50-year-old man. Slight posterior infarction, partial cardiographic recovery, anteroseptal infarction. (For necropsy findings see text.) *A*, Mainly R-T and T changes. *B*, Regression of changes and appearance of Q in Lead III. *C* and *D*, Anteroseptal infarction.

posterior cardiac infarction in cardiac failure following anterior transmural infarction (Fig. 1, *C* and *D*). Post-mortem examination showed patchy fibrosis of the myocardium of the posterior left ventricular wall with areas of softening due to atheroma of the right coronary branches. In contrast, there was a thrombotic occlusion of the anterior descending coronary artery responsible for extensive fibrosis of the septum and the anteromedial part of the left ventricle.

The absence of Q waves in the two severe cases was due to right bundle branch block in the first and to early recording (within a few hours after the infarction) in the second case.

3. *Septal Extension* (Posteroanterior cardiac infarction) is a feature of severe cardiac infarction. Absent in the slight and exceptional in the moderate cases, it was found in about one-third of the severe cases.

4. *Lateral Extension* was frequent in all three groups and may have been simulated in some by left ventricular hypertrophy.

5. *Arrhythmias, Complete Heart Block, and Bundle Branch Block* were absent in the slight and moderate cases. Their presence in twenty-four severe cases was related to septal extension of posterior infarction. The ten cases with temporary arrhythmias included auricular fibrillation (four cases), auricular flutter (one case), supraventricular paroxysmal tachycardia (two cases), ventricular paroxysmal tachycardia (one case), and runs of multiple ventricular extrasystoles (two cases). Heart block, complete or incomplete, was found in fourteen; six of these had associated bundle branch block (four right, two left).

6. *Electrocardiographic Restoration* is a feature of slight posterior cardiac infarction though it is less frequent than in anterior cardiac infarction. While less than one-fourth of the slight posterior infarctions showed a normal record at the end of two months, more than one-third of the slight anterior infarctions did so. Patients with slight posterior cardiac infarction who showed cardiograms reverting to normal all had horizontal hearts in which slight inversion of T in Leads III and aV_F may be physiologic. No records previous to infarction were available in four, and it may therefore be that these records of normal appearance were not normal for the individual patient. In the fifth case, restoration was complete. The records which improved in this group showed the changes of posterior coronary insufficiency in contrast to the severe group where the subacute changes of infarction often persisted. An extension of the lesion, which was usually laterally, occurred in equal proportions in the slight and severe groups. Three of the severe group died before a second electrocardiogram could be recorded.

7. *Mortality.*—No patients of the slight group died during the two months' period. Case 21 died suddenly three months after the attack and Case 14 developed congestive heart failure of which he eventually died, three and one-half years later. All survived the period of observation in the moderate group, but two died a few months later.

Severe posterior cardiac infarction, treated and untreated, had a mortality of 33 per cent. Out of the twenty-one who had anticoagulant treatment, fifteen recovered; out of the thirty-six old cases who had expectant treatment, only ten did so. Of the eighteen patients with posteroanterior infarction, eleven recovered and seven died; of the fourteen with heart block, twelve recovered and two died; of the ten with arrhythmias, eight recovered (including the only case with ventricular tachycardia) and two died. Eleven patients had posteroanterior infarction, heart block, and arrhythmias, and of these six recovered and five died.

POSTERIOR SUBENDOCARDIAL INFARCTIONS

Difficulty in classification was experienced in five patients. All five of these, after their first attack, had the same clinical symptoms of gradually worsening angina, as seen in impending cardiac infarction. In Cases 17, 68, and 85 the attack could be regarded as slight; in Case 74, where the patient had recently recovered from an extensive anterior infarction, it was severe. This patient died a fortnight after the electrocardiogram (Fig. 2) was recorded, and necropsy showed that death was due to acute posterior cardiac infarction. In Case 85 (Fig. 3) a severe posterior infarction occurred one week after the first record. The patient recovered, becoming free from symptoms. In Case 68 (Fig. 4) cardiac pain ceased under Tromexan treatment and the patient was discharged free of pain one month later. After three months, she developed severe posterior infarction and died eventually of congestive heart failure. In Case 17 (Fig. 5) the pain subsided within a few days of anticoagulant treatment. The patient returned to full work with no symptoms. Case 22 (Fig. 6) had no clinical episode of infarction; the patient had hypertension and angina of moderate severity and treatment is not completed at the present time. The electrocardiographic changes were similar in all. Flat and sagging R-T depression in Leads II, III, and aV_F of 1.5 to 2.5 mm. was the characteristic feature, associated with slight R-T elevation in aV_R in Cases 22, 68, and 85. There were no pathologic Q waves referable to posterior infarction in these first records; these only appeared when the severe transmural infarction developed (Figs. 3 and 4). Yet the result of the effort test in Case 17 proved that there was a severe injury present to produce on effort a pattern identical with acute posterior infarction. The test performed two months later gave normal results (Fig. 5). The electrocardiographic changes were those described as characteristic for subendocardial infarction.[21,22,23] Yu and Stewart[23] emphasized the rarity of pure posterior subendocardial infarction; they were able to record only one case among the seventeen they published (six with necropsy control) where R-T depression was seen in Leads II, III, and aV_F only. The common site is the anterolateral wall of the left ventricle and the cardiographic changes then appear in Leads I, II, aV_L, V_4, and V_5. Our only case of pure subendocardial infarction with necropsy control belonged to this group (Fig. 7) and the cardiographic changes, though in different leads, were similar to those found in Figs. 2, 3, 4, and 5. The steep depression of R-T in V_4 and V_5 may have been accentuated by small doses of digitalis, the T inversion by left ventricular hypertrophy. No Q waves were present.

DIAGNOSTIC AIDS TO SLIGHT POSTERIOR INFARCTION

The effort test has given further good results in slight posterior infarction when diagnosis was doubtful on routine recording. In Case 16 (Fig. 8) the patient had a normal pattern in Lead II and only borderline changes in aV_F; the R-T coving and T inversion in Lead III was regarded as insufficient evidence, in the presence of a horizontally placed heart, to confirm the diagnosis of posterior infarction. An effort test produced slight elevation of R-T and a monophasic T wave in Lead III, while the inverted T in aV_F became upright. After the pain

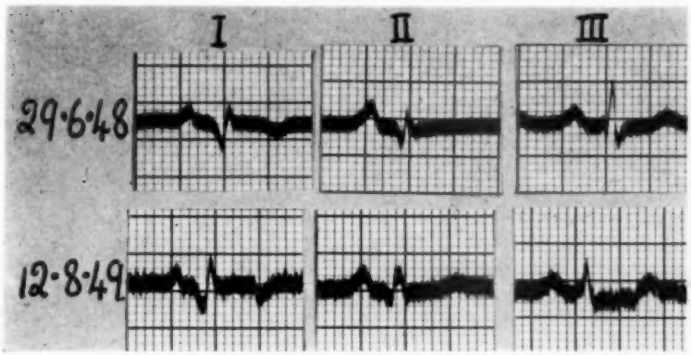


Fig. 2 (Case 74).—Electrocardiogram of a 43-year-old man. Posterior subendocardial infarction fourteen months after recovery from extensive anterior infarction. *A*, Record one month after anterior infarction. *B*, Fourteen months later the only new sign is a flat R-T depression in Lead III. The patient died ten days later of posterior transmural infarction.

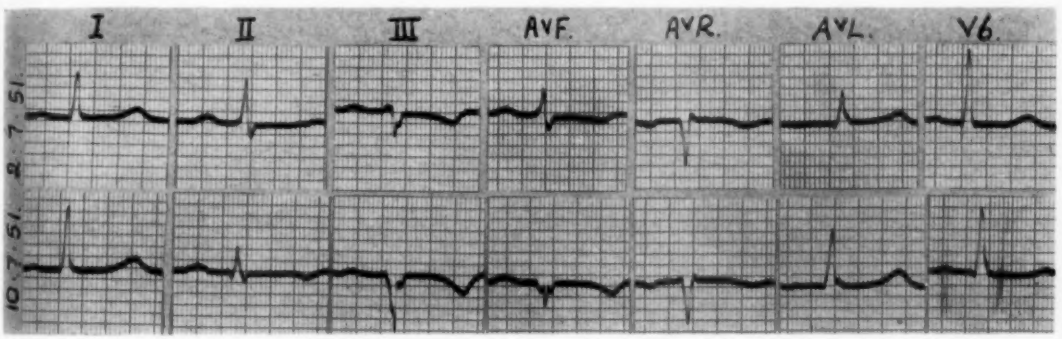


Fig. 3 (Case 85).—Electrocardiogram of a 60-year-old man. Posterior subendocardial infarction followed one week later by posterior transmural infarction. *A*, R-T depression in Leads II, III, and aV_F, with T inversion in Leads III and aV_F. *B*, Q waves in Leads II, III, and aV_F, R-T on the level, deepening of T inversion.

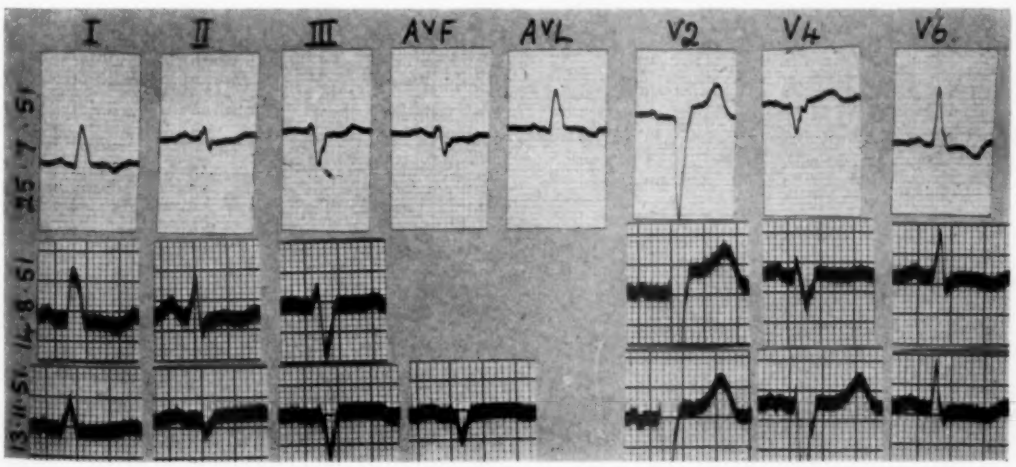


Fig. 4 (Case 68).—Electrocardiogram of a 45-year-old woman. Posterior subendocardial infarction, cardiographic recovery; three months later, posterior transmural infarction. *A*, Flat R-T depression in Leads II, III, and aV_F. Changes in anterior chest leads and aV_L caused by old anterior infarction. *B*, R-T at a level in Leads II and III. *C*, Appearance of Q waves in Leads II, III, and aV_F with acute R-T and T changes.

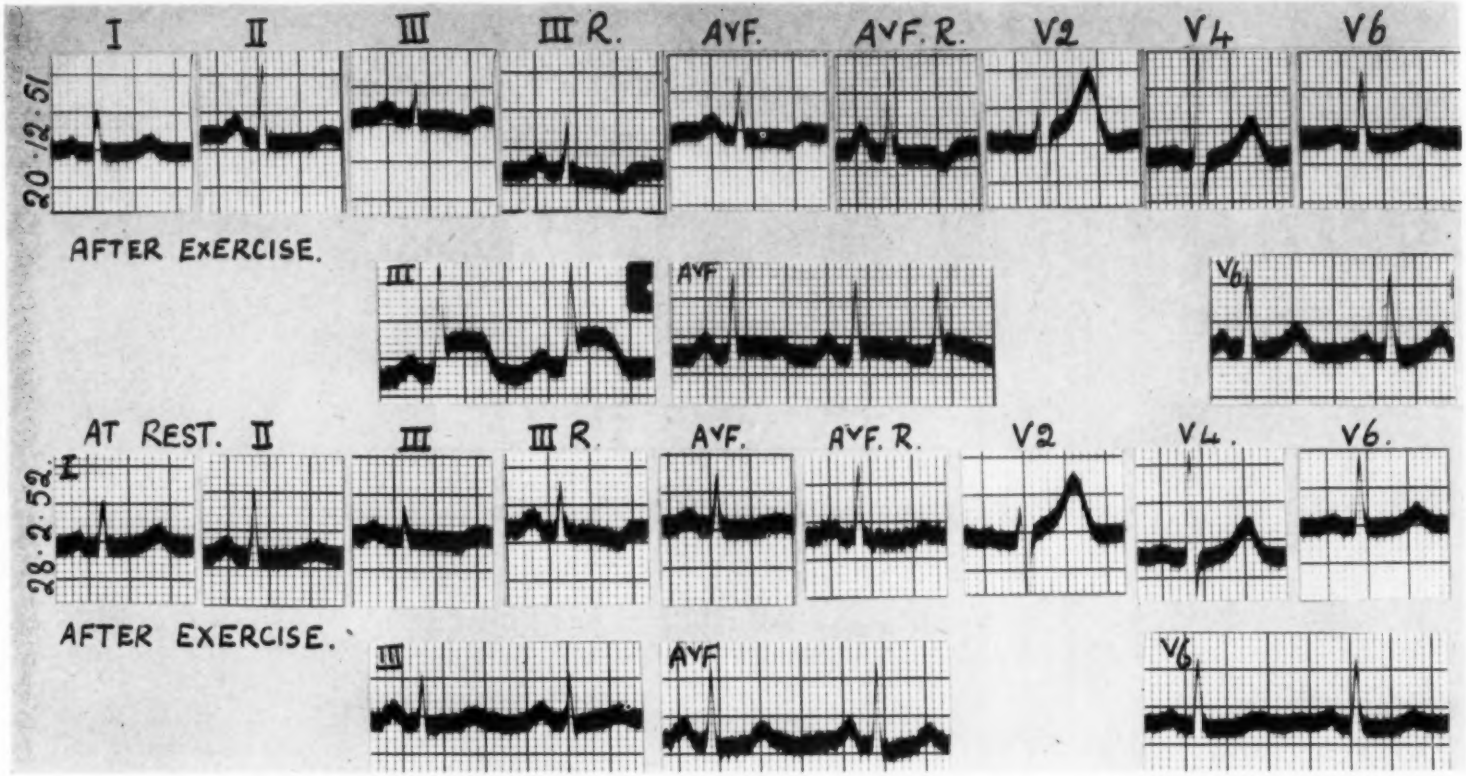


Fig. 5 (Case 17).—Electrocardiogram of a 60-year-old man. Posterior subendocardial infarction, acute subepicardial ischemia on exercise; two months later, partial cardiographic recovery with normal effort test. *A*, Changes in Leads II, III, and aV_F similar to those shown in Figs. 3 and 4; T inversion in Leads III and aV_F in deep inspiration (III R and aV_{FR}). On effort 4 mm. R-T elevation and monophasic T in Lead III, and to a lesser extent in aV_F. No change in V_6. *B*, R-T at a level: aV_{FR} and record after effort test remain normal.

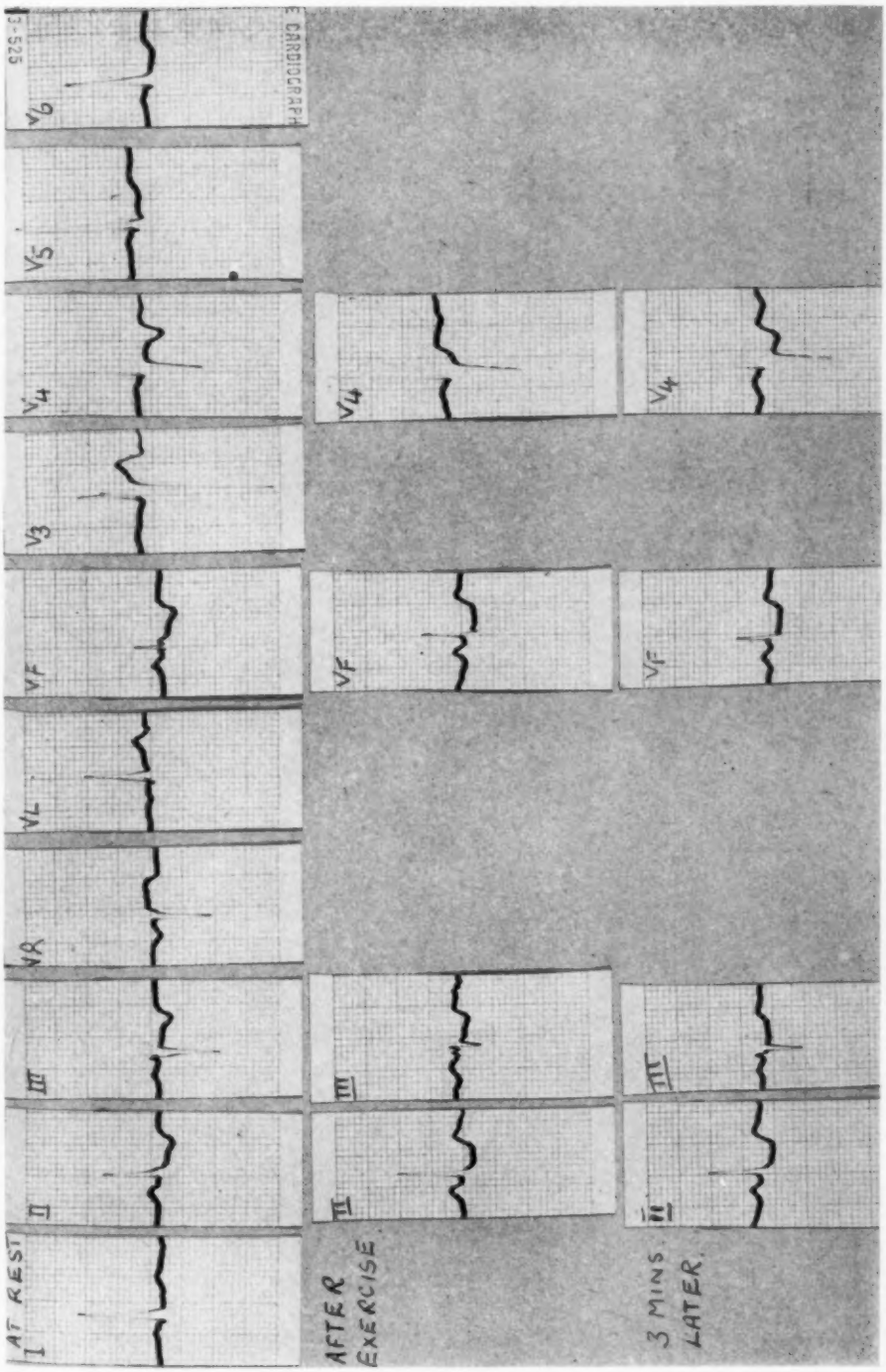


Fig. 6 (Case 22).—Posterior subendocardial infarction during recovery from slight anterior infarction. Note R-T elevation in aV_R and absence of Q waves. Left ventricular strain. On effort, deepening of R-T depression in posterior leads; paradoxical reversal of T in V_4.

had subsided with trinitrin and the record reverted to its resting pattern, a small Q in Lead III appeared. A different result is shown in Fig. 9, with a posterior scar pattern, in which the effort test produced a left bundle branch block in the patient. Time often clinched the diagnosis. In Fig. 10, the lateral changes

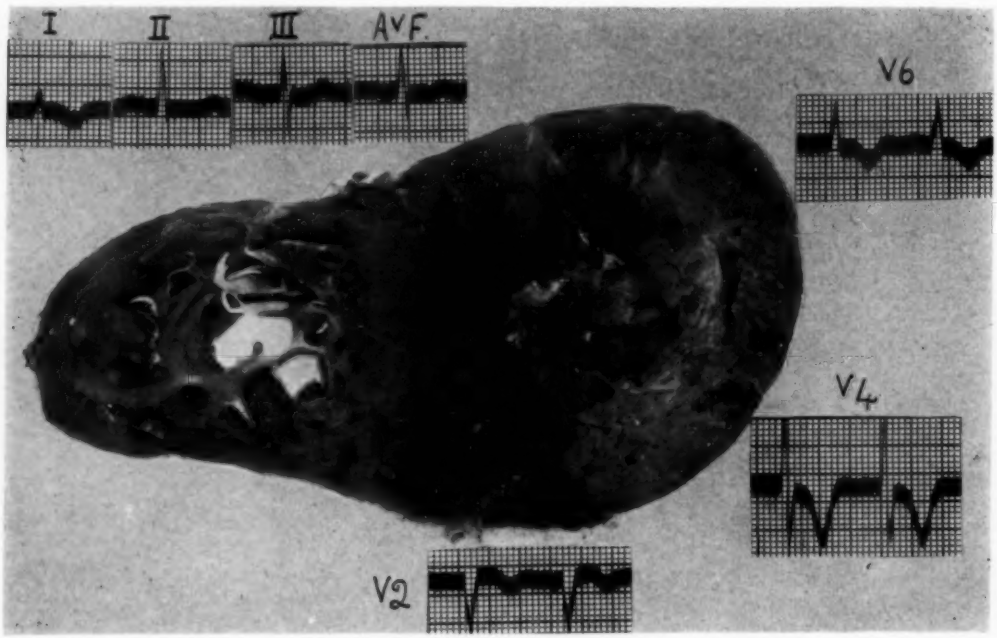


Fig. 7 (Case SM).—Electrocardiogram of a 75-year-old woman. Anterolateral subendocardial infarction in hypertensive heart disease with auricular fibrillation. Sudden death three weeks after infarction; severe narrowing of coronary arteries without occlusion. Steep R-T depression in V_4 caused by subendocardial fibrosis; deep T inversion is a combined effect of subepicardial fibrosis and left ventricular hypertrophy. Uninjured strip of myocardium surrounding infarcted area prevents appearance of Q waves.

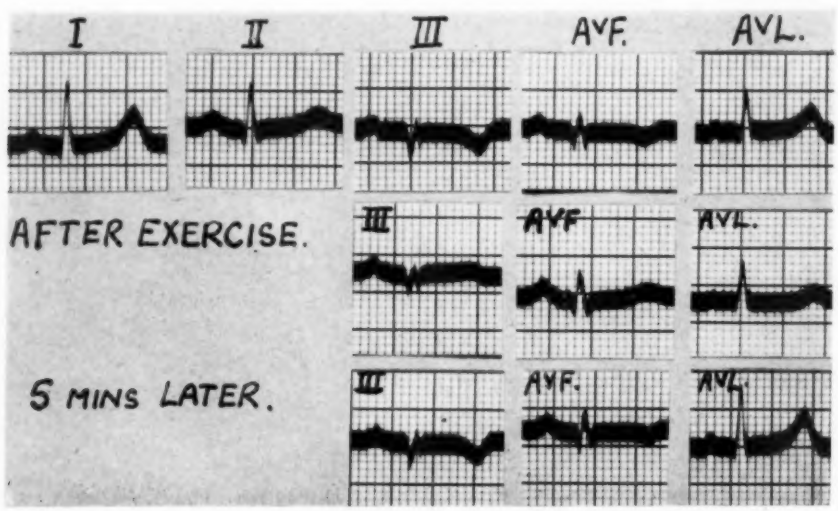


Fig. 8 (Case 16).—Electrocardiogram of a 45-year-old man. Slight posterior subepicardial infarction in horizontal heart. After exercise R-T elevation and monophasic T in Lead III; five minutes later, Q in Lead III. Paradoxical reversal of T in aV_F. No change in aV_L.

were regarded as more important in the first record, while the posterior changes were doubtful. Two months later, progressive changes in Lead II, the appearance of Q in Lead III which deepened in Lead III R and was carried into Lead aV_F, made the diagnosis of posterior infarction certain.

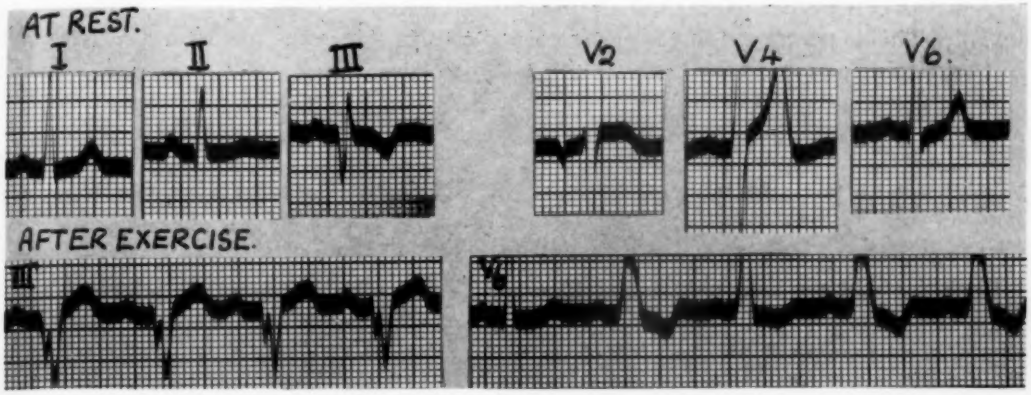


Fig. 9 (Case 7).—Electrocardiogram of a 63-year-old man. Healed posterior infarction. Severe angina. After exercise septal ischemia with appearance of left bundle branch block.

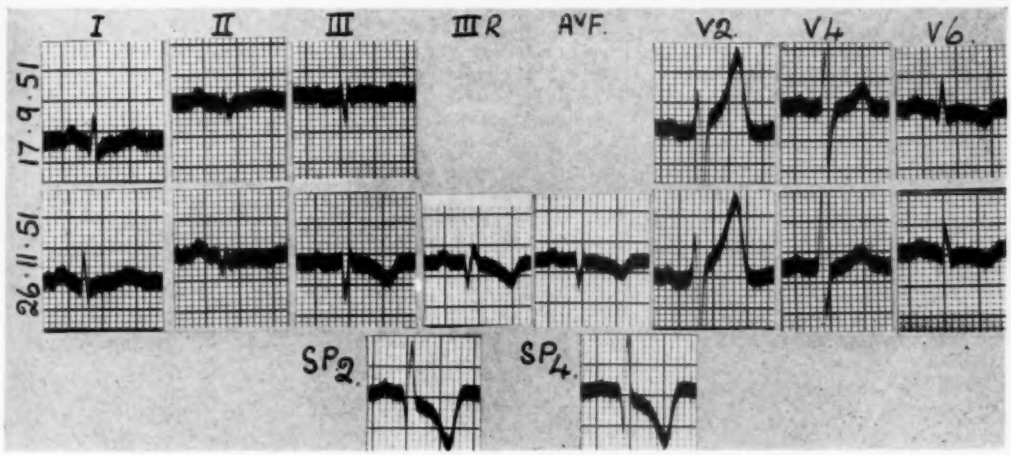


Fig. 10 (Case 15).—Electrocardiogram of a 57-year-old man. Slight posterolateral infarction; the heart is horizontal. *A*, R-T bowing and T inversion in V_6; dubious changes in Leads II and III. *B*, Two months later Q in Leads II and III and aV_F, accentuated in III R. (For "S.P." leads see text.)

The bipolar leads proposed by Slapak and Partilla ("S.P." leads) proved disappointing. Admittedly they magnify the R-T and T changes in Leads III and aV_F and show deeper Q waves than in the classical leads. But these Q waves are different; they are narrow, smooth, and do not show the notching and slurring so characteristic of the epicardial Q in Lead III in posterior cardiac infarction (Fig. 10). That they are the physiologic intracardiac potentials derived through the mitral orifice is further proved in Fig. 11. In this normal record of a semi-horizontal heart, Q in SP_4 position is as deep as R is high and is followed by an inverted T. This record refutes the statement of these authors that Q in these leads under normal conditions is never more than one-fifth of the following R.

DIAGNOSIS OF SEVERE POSTERIOR INFARCTION

The Q III-T III pattern carried into aV_F, also apparent in Lead II[24] is the well-recognized pattern of posterior infarction; however, it is not the earliest one. Before it appears, oblique elevation of the R-T period with huge T waves but no Q waves can be recorded from the infarcted epicardial surface of the posterior wall. This is portrayed in Fig. 12, recorded a few hours after the attack started; it persisted for more than twenty-four hours. The acute pattern was seen only two days later, when a minute Q appeared in Lead III (Fig. 12,*B*). Dressler and Roesler[25] who described this pattern, thought to be due to release of potassium

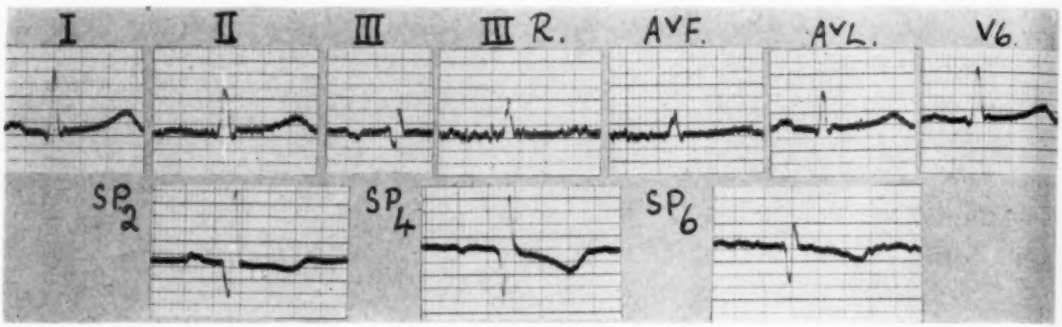


Fig. 11 (Case VE).—Electrocardiogram of a 58-year-old man. Normal record in a semihorizontal heart; dubious Q disappears in Lead III R. "S.P." leads abnormal.

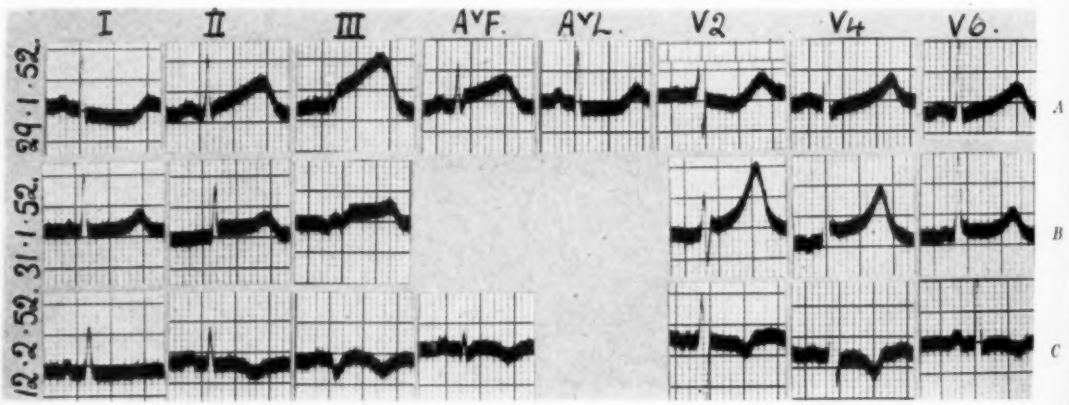


Fig. 12 (Case 100).—Electrocardiogram of a 74-year-old woman, showing earliest changes were in extensive posterior infarction. *A*, Steep R-T elevation in Leads II, III, and aV_F fused with giant T in Lead III; no Q waves. Reciprocal R-T depression in Leads I, aV_L, and V_2. *B*, Temporary appearance of tall secondary T in V_2 and V_4, though R-T elevation suggests anteroseptal involvement as well. *C*, Disappearance of secondary T waves and R-T; T changes V_2-V_6 diagnostic of posteroanterior infarction.

from the injured cells, believed that when it persists for longer than twenty-four hours it was of a bad prognostic significance. The 75-year-old patient in Fig. 12 made an uneventful recovery. The high T of the initial stage derived from the infarcted area should not be confused with the tall T in the anterior chest leads and Lead I derived as a reciprocal electrical effect from the uninjured surface of the left ventricle. At one or other stage of severe posterior infarction, this secondary effect almost always appears and then may persist for weeks. These tall T waves are preceded during the early stages by R-T depression in the same leads

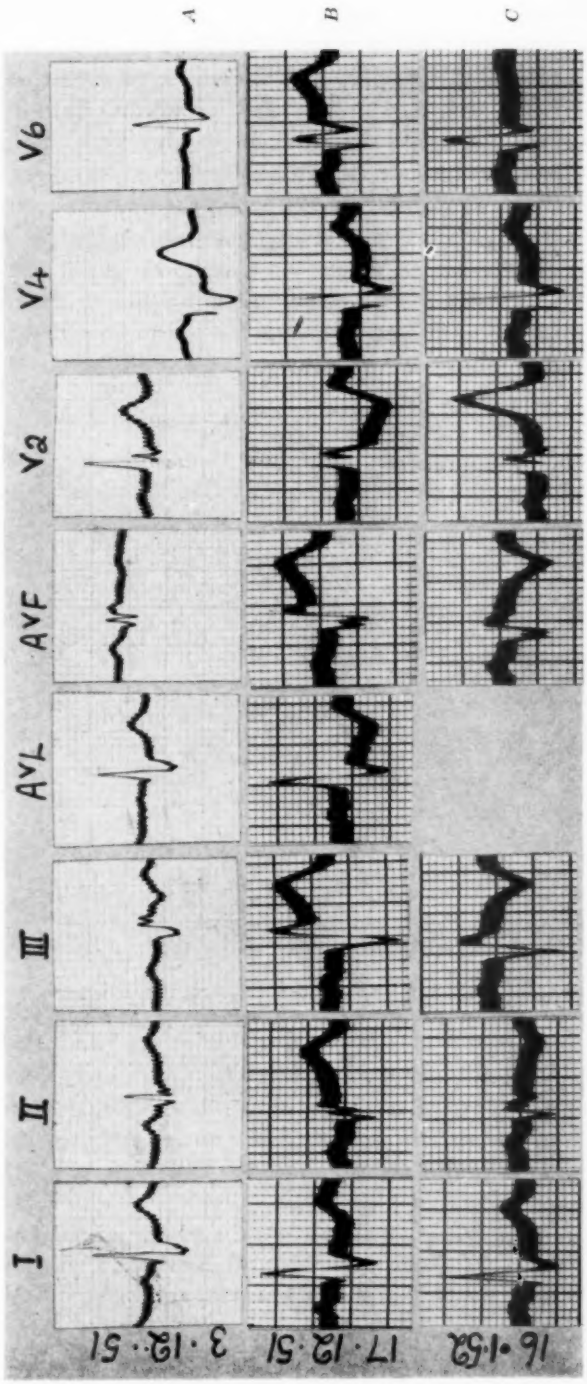


Fig. 13 (Case 86).—Electrocardiogram of a 75-year-old woman. Posterior infarction in presence of right bundle branch block. *A*, Broad Q in Lead III, presence of Q in Leads II and aV_F and acute R-T and T changes in Leads III and aV_F diagnostic. *B*, Further posterior extension fortnight later. R-T depression aV_L and V_2 a secondary effect as proved in *C* by tall secondary T in V_2 which excludes anterior extension.

(Fig. 12). R-T depression at this stage may be due to anterior subendocardial infarction as well, and may be therefore the earliest sign of posteroanterior infarction. Subsequent records will prove the diagnosis. If, in place of R-T depression, tall T waves appear in Leads I, aV_L, V_5, and V_4 it is certain that only posterior infarction has occurred (Fig. 13). If bowing of R-T and inversion of T develops in these leads as well, the diagnosis of simultaneous anterior infarction will be certain. The appearance of the latter pattern may be sometimes delayed, for several days may pass before the infarction reaches the anterior ventricular surface and in the meantime, tall T waves may appear temporarily, as in Fig. 12,*B*; but the crescentric R-T elevation in V_4 and V_6 in this patient left little doubt of anterior involvement as proved by successive records (Fig. 12,*C*). On records previously abnormal through left ventricular strain or anterior or anterolateral infarction, the summation effect of tall T upon inverted T waves may produce

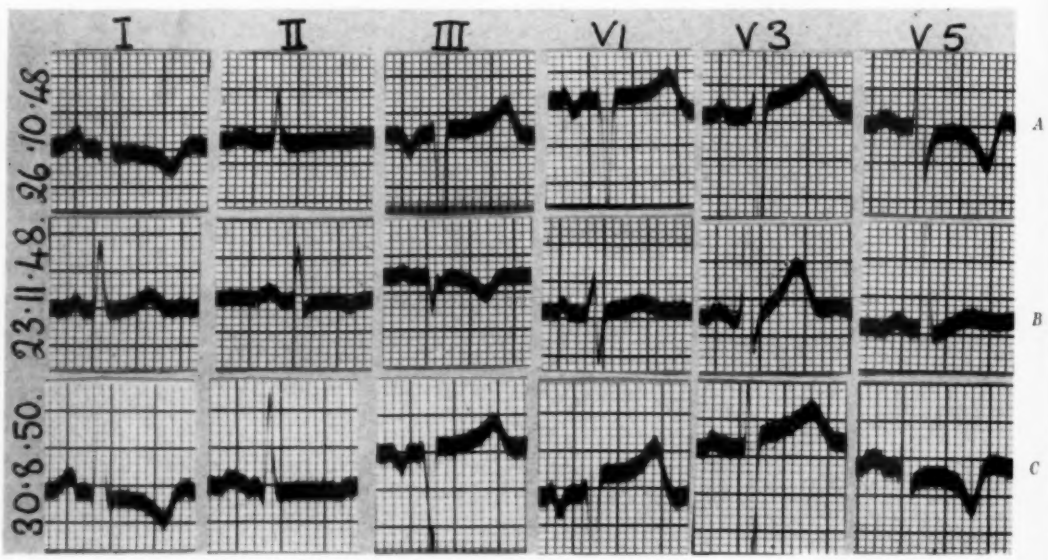


Fig. 14 (Case 3).—Electrocardiogram of a 66-year-old man. *A*, Severe left ventricular strain pattern. *B*, Obliterated by posterior infarction. *C*, Two years later reversal to *A* with no signs of posterior infarction.

odd pictures. Severe left ventricular strain may disappear; it may show up again and the record may revert entirely to its previous pattern after the posterior infarction has healed (Fig. 14). Signs of previous anterolateral infarction may become temporarily obliterated. On a superficial glance these records may look more normal; as Graybiel and White[23] remarked, ". . . the heart is actually more damaged than before, there being now two infarctions instead of one."

DISCUSSION

The R-T and T changes observed in cardiac infarction are the signs of muscle injury, while the appearance of Q waves derived from the epicardial surface is the sign of muscle necrosis. Injured muscle produces electric potential ("injury current"), dead muscle does not; this, therefore, enables the recording of the

normal intracavitary potential, the Q wave, through the epicardium. Thus the question is pertinent—whether in the absence of the electrocardiographic signs of muscle necrosis (epicardial Q waves) the diagnosis of cardiac infarction is permissible.

Q is only a sign of cardiac infarction in so far as it is a sign of transmural infarction. In slight cardiac infarction due to patchy necrosis, whether anterior or posterior, no large bridge of dead tissue may form through which Q waves can be recorded from the epicardium. The infarcted area may either be subepicardial, subendocardial, or intramural. The small areas may coalesce into larger and deeper ones and so may become transmural in limited areas, a Q wave may then appear. The electrocardiographic signs of R-T displacement and T inversion follow the rules established in animal experiments by the production of myocardial injury at various levels by Wolferth, Bellett, Livezey, and Murphy,[27] Pruitt and Valencia,[28] and Hellerstein and Katz.[29] Subepicardial injury produces R-T elevation and terminal T inversion;[30] subendocardial injury produces R-T depression over the epicardium of the injured area and R-T elevation in the cavitary aV_R lead, accompanied later by T-wave changes.

The degree of R-T displacement will depend on the extent of injury and on the spatial orientation of the injured area relative to the electrodes. The electrical field of a limited injury may be brought into the radius of the electrodes by three different means: (1) by displacement of the electrodes; (2) by displacement of the heart, and (3) by temporary extension of the field of injury. The first of these produced Lead aV_F and the esophageal leads but other chest leads did not add anything to the diagnosis. The second way proved successful in the hand of Evans,[14] and several of our figures prove the usefulness of Lead III R; but in the case of limited injury to the posterior basal part of the left ventricle, the rotation of the heart in deep inspiration may obliterate the abnormal signs by bringing the healthy part of the left ventricle into the electrical field, in the same way that changes in bodily posture may show or obliterate the signs of old posterior infarction in the limb leads.[31]

Effort test, the third way, though extensively applied in the diagnosis of coronary insufficiency, has not been used to localize coronary changes. All authors confirm that V_4 and V_5 are the elective leads to record ischemic R-T changes and that Lead III is unreliable, for T frequently changes here in amplitude and direction in normal controls.[32-35] Evans and Bourne[36] found only a few instances where the response of the test has given a characteristic localizing change. Master[13] observed occasional RS-T elevation in Lead III, or in Leads II and III, after his two-step exercise, where Q in Leads II or III was present in the resting electrocardiogram in patients " . . . in whom the posterior surface of the left ventricle is susceptible to anoxaemia." Burchell, Pruitt, and Barnes[37] recorded after the anoxemia test unipolar limb leads and found maximal R-T depression in aV_F in a few cases where the heart was vertical and in aV_L when it was horizontal. R-T elevation in aV_R proved that ischemia was greatest in the subendocardial areas.

The application of the effort test to our cases with posterior subendocardial infarction produced an extension of the ischemic zone to the epicardium, as shown

by the upwards displacement of R-T in Leads III and aV_F in Case 17 (Fig. 5) or in the subendocardium, as shown by deepening of the R-T depression in the posterior leads (Fig. 6). The uprighting of the inverted T wave in aV_F (Fig. 8) has to be regarded as abnormal, and such a paradoxical effect has since been observed in other similar cases. We believe that this is due to endocardial extension of subepicardial ischemia producing intracavitary potential changes responsible as a secondary effect for the "paradoxical reversal"[38] of the previously inverted epicardial T wave.[39]

Since slight posterior infarction has such a good prognosis, its diagnosis may be thought to be of academic interest. This is not so. If the clinical signs of gradually worsening angina of effort and at rest herald an impending infarction, the electrocardiogram can prove that this has, in fact, already started. We were able to show that anticoagulant treatment applied at this stage may ward off a severe infarction.[40] Some of our cases here mentioned confirm this view. In Cases 16 and 17 infarction did not progress any further. In Case 68, severe infarction supervened, but only three months after the completion of treatment. In Case 85, which was treated at another hospital, no effective prothrombin levels were obtained during the first week, at the end of which severe infarction developed. In Case 74 (our earliest patient), heparin was started a fortnight after the electrocardiographic signs appeared. The patient died on the third day of treatment. The electrocardiographic signs of slight posterior infarction, magnified by effort test, thus add further weight to the clinical signs of impending cardiac infarction making anticoagulant treatment a necessity.

SUMMARY

In a consecutive series of one hundred patients with posterior cardiac infarction assessed according to severity of the attack, 22 per cent were slight, 21 per cent moderate, and 57 per cent severe. This was in contrast to anterior cardiac infarction where this incidence was 42.2 per cent, 22.6 per cent, and 35.2 per cent, respectively. Greater gravity in posterior infarction can be explained by the frequency of arrhythmias and by the tendency of some slight posterior infarctions to become severe, a development exceptional in slight anterior infarction.

In slight posterior cardiac infarction, the following electrocardiographic patterns were shown: absent pathologic Q waves in more than one-half the cases; R-T and T changes of the subacute type, for example, bowed R-T with isoelectric take-off and deep inversion of T; and electrocardiographic restoration in about one-fourth of the cases. The severe cases, in contrast, exhibited pathologic Q waves in almost every instance; an acute pattern, for example, high R-T take-off and monophasic T wave in the great majority, and arrhthmias were found in more than one-third of the cases. In the moderate group, the incidence of these signs was transitional, except that no arrhythmias were observed. There was no mortality in the slight and moderate group during the first two months. The mortality in the severe group of treated and untreated cases was 33 per cent.

The diagnostic difficulties in slight posterior cardiac infarction were solved by effort test, Leads III R and aV_{FR}. Recent bipolar leads advised for posterior infarction proved disappointing. No diagnostic problems have arisen in the

moderate and severe cases. The absence of secondary T-wave changes in anterior chest leads proved an important point in the diagnosis of posteroanterior cardiac infarction.

In five patients, slight cardiac infarction was followed by increasingly severe angina; two of these developed severe posterior cardiac infarction within a fortnight and one of them died. Early anticoagulant treatment appeared to delay the severe attack by months in one patient, while in the other two it seemed to prevent it. All the five showed electrocardiographic signs suggesting posterior subendocardial infarction, consisting in sagging or flat R-T depression in Leads II, III, and aV_F. Effort test caused temporary extension of ischemia and transformed these dubious records into unequivocal ones. This result was considered an important indication for prompt anticoagulant treatment.

The authors are indebted to Miss Anne Smith for taking and mounting the electrocardiograms, and for her technical assistance.

REFERENCES

1. Papp, C., and Smith, K. Shirley: Electrocardiographic Patterns in Slight Coronary Attacks, Brit. Heart J. **13**:17, 1951.
2. Papp, C., and Smith, K. Shirley: Prognosis and Treatment of Cardiac Infarction, Brit. M. J. **1**:1471, 1951.
3. Goldberger, E.: Unipolar Lead Electrocardiography, ed. 2, Philadelphia, 1949, Lea & Febiger.
4. Myers, G. H., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Anteroposterior Infarction, Am. Heart J. **37**:205, 1949.
5. Scherf, D., and Boyd, L. J.: Clinical Electrocardiography, ed. 3, London, 1948, William Heinemann, Ltd.
6. Myers, G. B., and Oren, B. G.: The Use of the Augmented Unipolar Left Leg Lead in the Differentiation of the Normal From the Abnormal Q Wave in Standard Lead III, Am. Heart J. **29**:708, 1945.
7. Bain, C. W. C.: The Oesophageal Lead, Brit. Heart J. **13**:485, 1951.
8. Oram, S., Holt, M., and East, T.: Oesophageal and Other Leads in Posterior Cardiac Infarction, Brit. Heart J. **13**:475, 1951.
9. Rosenbaum, F. F., Wilson, F. N., and Johnston, F. D.: The Precordial Electrocardiogram in High Lateral Infarction, Am. Heart J. **32**:135, 1946.
10. Sears, C. H., and Myers, G. B.: Diagnosis of Posterior Infarction With the Aid of Semidirect Leads From the Back and Oesophagus, Am. J. Med. **8**:808, 1950.
11. Slapak, L., and Partilla, H.: Zur elektrokardiographischen Diagnostik des Hinterwandinfarktes, Wien. Ztschr. Inn. Med. **30**:425, 1949.
12. Slapak, L., and Partilla, H.: The Diagnosis of Posterior Wall Infarction and of Aneurysm of the Posterior Wall in the Electrocardiogram, Acta med. Scandinav. **139**:42, 1950.
13. Nehb, W.: Das Brustwand-Elektrocardiogram, Verhandl. d. deutsch. Gesellsch. f. Kreislaufforsch. **12**:177, 1939.
14. Evans, W.: The Effect of Deep Inbreathing on Lead III of the Electrocardiogram, Brit. Heart J. **13**:457, 1951.
15. Wood, P., McGregor, M., Magidson, O., and Whittaker, W.: The Effort Test in Angina Pectoris, Brit. Heart J. **12**:363, 1950.
16. Master, A. M.: The Two Step Exercise Electrocardiogram: A Test for Coronary Insufficiency, Ann. Int. Med. **32**:842, 1950.
17. Papp, C.: Acute Cardiac Infarction Without Pain, Brit. Heart J. **14**:250, 1952.
18. East, T., and Oram, S.: The Cardiogram in Ventricular Aneurysm Following Cardiac Infarction, Brit. Heart J. **14**:125, 1952.
19. Coelho, E., Borges, A. S., Barata, M. I., Esá, B., and Maltez, J.: L'évolution clinque et électrocardiographique de 320 cas d'infarctus du myocarde. Les potentiels intracardiaques dans l'infarctus, Arq. brasil. cardiol. **3**:445, 1950.
20. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Posterior Infarction, Am. Heart J. **38**:547, 1949.
21. Price, R. K., and Janes, L. R.: A Case of Subendocardial Infarction, Brit. Heart J. **5**:134, 1943.
22. Levine, H. D., and Ford, R. V.: Subendocardial Infarction; Report of Six Cases and Critical Survey of the Literature, Circulation **1**:246, 1950.

23. Yu, P. N. G., and Stewart, J. M.: Subendocardial Myocardial Infarction With Special Reference to Electrocardiographic Changes, Am. Heart J. **39**:862, 1950.
24. Evans, W., and Hunter, A.: Chest Lead CR7 in Cardiac Infarction, Brit. Heart J. **5**:73, 1943.
25. Dressler, W., and Roesler, H.: High T Waves in the Earliest Stage of Myocardial Infarction, Am. Heart J. **34**:627, 1947.
26. Graybiel, A., White, P. D., Wheeler, L., and Williams, C.: Electrocardiography in Practice, ed. 2, London-Philadelphia, 1946, W. B. Saunders Company.
27. Wolferth, C. C., Bellet, S., Livezey, M. M., and Murphy, F. D.: Negative Displacement of the RS-T Segment in the Electrocardiogram and Its Relationships to Positive Displacement: An Experimental Study, Am. Heart J. **29**:220, 1945.
28. Pruitt, R. D., and Valencia, F.: The Immediate Electrocardiographic Effects of Circumscribed Myocardial Injuries; An Experimental Study, Am. Heart J. **35**:161, 1948.
29. Hellerstein, H. K., and Katz, L. N.: Electrical Effects of Injury at Various Myocardial Locations, Am. Heart J. **36**:184, 1948.
30. Brink, A. J., and Goodwin, J. F.: Significant Observations on the Precordial T Deflection of the Electrocardiogram, Brit. Heart J. Brit. Heart J. **14**:331, 1952.
31. Brofman, B. L., Feil, H., Hellerstein, H. K., and Jones, A. M.: Postural Electrocardiographic Changes in Healed Myocardial Infarction, Circulation **3**:752, 1951.
32. Barrow, W. H., and Over, R. A.: Electrocardiographic Changes With Exercise, Arch. Int. Med. **71**:547, 1943.
33. Unterman, D., and DeGraff, A. C.: The Effect of Exercise on the Electrocardiogram (Master "Two Step" Test) in the Diagnosis of Coronary Insufficiency, Am. J. M. Sc. **215**:571, 1948.
34. Grossman, M., Weinstein, W. W., and Katz, L. N.: The Use of the Exercise Test in the Diagnosis of Coronary Insufficiency, Ann. Int. Med. **30**:387, 1949.
35. Scherlis, L., Sandberg, A. A., Wener, J., Dvorkin, J., and Master, A. M.: The Effects of the Single and Double "Two-Step" Exercise Test Upon the Electrocardiogram of 200 Normal Persons, J. Mt. Sinai Hosp. **17**:242, 1950.
36. Evans, C., and Bourne, G.: Electrocardiographic Changes After Anoxaemia and Exercise in Angina of Effort, Brit. Heart J. **3**:69, 1941.
37. Burchell, H. B., Pruitt, R. D., and Barnes, A. R.: The Stress and the Electrocardiogram in the Induced Hypoxemia Test for Coronary Insufficiency, Am. Heart J. **36**:373, 1948.
38. Hecht, H. H.: On Changes of the T Wave and the RS-T Segment of the Human Electrocardiogram, Am. Heart J. **37**:639, 1949.
39. Pruitt, R. D., Burchell, H. B., and Essex, H. E.: Derivations of the RS-T Segment in Acute Subendocardial Injuries, Circulation **4**:108, 1951.
40. Smith, K. Shirley, and Papp, C.: The Prevention of Impending Cardiac Infarction by Anticoagulant Treatment, Brit. Heart J. **13**:467, 1951.

THE MECHANISM OF COMPLETE AND INCOMPLETE BUNDLE BRANCH BLOCK

María Isabel Rodriguez, M.D., and Demetrio Sodi-Pallares, M.D.

Mexico, D. F., Mexico

IN a recent publication,[1] we reported our studies on the process of activation of the interventricular septum in the dog's heart. Our results were somewhat different from the classically accepted ideas on the subject, and they permitted us to conclude that the average direction of the process of activation in the interventricular septum took place from left to right and from below upward. The first portions activated in the septum (the earliest in the entire cardiac cycle) were in the middle of the left septal surface. The remainder of this surface and then almost all the thickness of the interventricular septum formed mainly by the left ventricle were activated later (around 0.01 second).

On the right septal surface, the first portions activated (0.01 second after onset of activation of the left side) corresponded to the base of the anterior papillary muscle, and the latter, to the regions proximal to the insertion of the tricuspid and pulmonary valves. The left septal surface, almost all the thickness of the septum, and even some portions of the right septal surface, depended for their activation on the left branch of the bundle of His. Indeed, it was proved that the activation of these portions were not delayed when the right bundle of His was severed. If the left branch were sectioned, a delay took place in this region. The remaining portions of the right septal surface depended for their activation on the right bundle branch.

Considering the usefulness and the simplicity of the procedure employed in the experimental work mentioned above,[1] we decided to study the modifications that the different degrees of bundle branch block produce in the propagation of the wave of activation in the interventricular septum.

METHOD

Dogs were anesthetized with Nembutal with a dose of 35 mg. per kilogram of body weight. The open chest method with artificial respiration was used. The electrodes used and the manner in which they were introduced were similar to those described in the previous paper.[1]

In the experiments, unipolar, in addition, proximal bipolar, and distant bipolar leads were recorded, always simultaneously with Lead II. Unipolar leads are, generally speaking, the most useful to determine through which branch

From the Department of Electrocardiography of the Instituto Nacional de Cardiología de México.
Received for publication July 15, 1952.

of the bundle the explored points receive their activation (consult Method in previous paper).[1] The two types of bipolar leads used most are illustrated in the drawings adjoining the figures. In the first type of bipolar leads, the two sites for the lead are given in the drawings as points *A* and *B*. Electrode A was placed on the left septal surface and it always registered negative polarity, whereas electrode B, placed within the thickness of the septum, had positive polarity. The distance between both was variable, from 5 to 6 or more millimeters. The characteristic of this first group of bipolar leads was that both electrodes were placed at points which depend for their activation on the left branch of the bundle of His. The second type of bipolar leads, called transeptal leads, were placed with the points of contact, one on the left septal surface (*C*) with negative polarity, and the other on the right septal surface (*D*) with positive polarity; the latter depended for its activation on the right bundle branch. With the mentioned connections, both in bipolar leads between septal points and in transeptal leads, the registration of a positive deflection implies that the path followed by the wave of activation at that site is from left to right or at least that in general terms the process of activation has such a direction.

The technique for the section of the branches of the bundle of His was similar to that described in previous papers.[2,3]

RESULTS

1. *Right Bundle Branch Block.*—

A. A study was made first of the wave of activation in the septal muscle belonging to the left ventricle (the major part of the septal musculature), when right bundle branch block is produced. This study was carried out using unipolar and bipolar leads at various levels. The results were uniform and are analogous to those illustrated in Fig. 1.

In the experiment illustrated in this figure, four points in the left septum were explored: points *A* and *A'* on the endocardium of the left surface of the septum and points *B* and *B'* at 5 mm. below this surface at the sites indicated in the attached schema. In this figure are shown the unipolar leads (upper and middle rows in Columns 1, 2, 4, and 5) and relative close bipolar leads (upper and middle tracings in Columns 3 and 6) recorded between the left septal points, before and after producing right bundle branch block. All of these are simultaneous with Lead II (lower row). In the control tracing (Columns 1, 2, and 3) the morphology of the direct leads is what is usually encountered: the intrinsic deflection of the unipolar leads is inscribed early in relation to QRS in Lead II, and the bipolar leads are predominantly positive and of rapid inscription. Right bundle branch block does not alter the morphology of the direct leads (Columns 4, 5, and 6). The inscription of the intrinsic deflection of the unipolar leads and the upper peak of the bipolar leads continue to be early and their relations with regard to the beginning of QRS in Lead II are the same as those of the control tracing.

In the previous experiment we noted that the direction and sequence of activation in the left septal mass were not modified with right bundle branch block.

The speed of conduction between points *A* and *B* and between *A'* and *B'* is about 1,000 mm. per second, under control conditions as well as after the production of right bundle branch block. Similar results are produced if the electrodes are moved farther apart, the distance not being important as long as the zones explored by the electrodes are activated by the left bundle branch.

B. When the bipolar leads were transeptal, the results were different. In the experiment illustrated in Fig. 2, the control tracings are shown in Column 1 and include a transeptal lead obtained at the level marked in the adjoining sketch. Standard Lead II (uppermost tracing) was recorded simultaneously with the unipolar lead of the right septal surface at point *D* (second tracing), in which it is seen that the vertex of the intrinsic deflection occurs between 0.01 and 0.0125 second after the beginning of QRS in Lead II. The unipolar lead of the left septal surface at point *C* (third tracing) was recorded simultaneously with the previous tracings; in it, the inferior vertex of the intrinsic deflection is synchronous with the beginning of QRS in Lead II. The lowest tracing shows the bipolar transeptal Lead C-D simultaneous with the three previous tracings; it is entirely positive and its vertex occurs at a time intermediate between those of the intrinsic deflections of the left and right septal unipolar leads. The control tracings we have described are highly illustrative, since they show the promptness with which the activation take place on the left septal surface; the beginning of the corresponding intrinsic deflection occurs before the onset of QRS in Lead II but its lower vertex is coincident with it. Activation of the right septal surface takes place 0.01 second later.

In Column 2 the same leads following the production of right bundle branch block are shown. The unipolar lead of the right septal surface at point *D* (second tracing) is of the rsRS type and the lower vertex of the intrinsic deflection is inscribed around 0.06 second after the beginning of QRS in Lead II. The left septal unipolar lead at point *C* (third tracing) shows the same sequence as that seen in the control tracing, and its intrinsic deflection has the same relation to the beginning of QRS in Lead II that existed before the block. The transeptal bipolar Lead C-D (lowest tracing) has widened considerably and shows a plateau in its upper portion. The ascending limb of this tracing is synchronous with the intrinsic deflection of the right septal unipolar lead.

It may be assumed that there is a considerable difference between the times of arrival of the wave of activation to the two septal surfaces.

C. In order to study the changes that take place in the transeptal leads at different levels of the interventricular septum, experiments similar to those illustrated in Fig. 3 were done. Two transeptal leads were registered, one in the inferior one-third of the septum between points *C* and *D*, and the other in the superior one-third of the septum between the points *C'* and *D'*. In Column 1 (uppermost tracing) standard Lead II (control) registered simultaneously with the bipolar transeptal Lead C-D (middle tracing), and with the bipolar transeptal Lead C'-D' (lowest tracing), is shown. The vertex of the bipolar Lead C-D is recorded from 0.01 to 0.015 second after the beginning of QRS in standard Lead

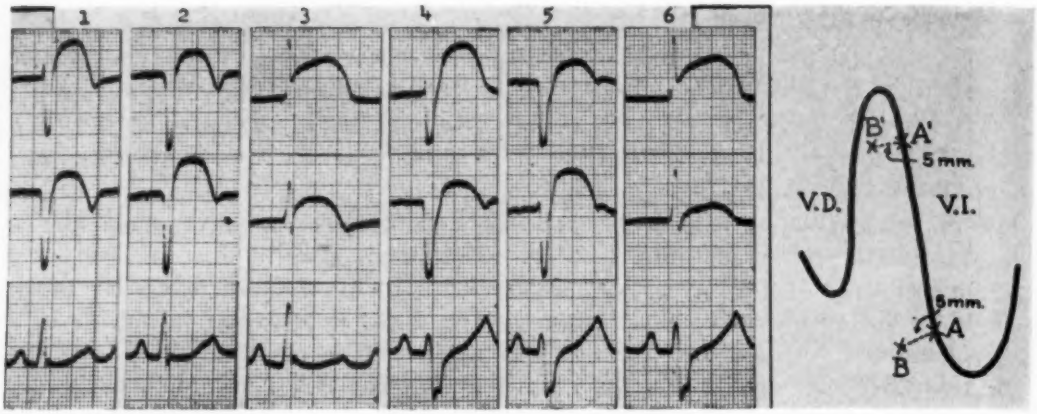


Fig. 1.—Unipolar and bipolar leads taken at the four left septal points indicated in the adjoining drawing. *1*, Control tracings: unipolar leads from point *B* (upper tracing) and from point *A* (middle tracing), simultaneous with Lead II (lower tracing). *4*, The same leads as in *1* after producing right bundle branch block. *2*, Control tracings: unipolar leads from point *A'* (upper tracing) and from point *B'* (middle tracing) simultaneous with Lead II (lower tracing). *5*, The same leads as in *2* after producing right bundle branch block. *3*, Control tracing: bipolar lead between *A* and *B* (upper tracing) simultaneous with the bipolar lead between *A'* and *B'* (middle tracing) and with Lead II (lower tracing). *6*, The same leads as in *3* after producing right bundle branch block.

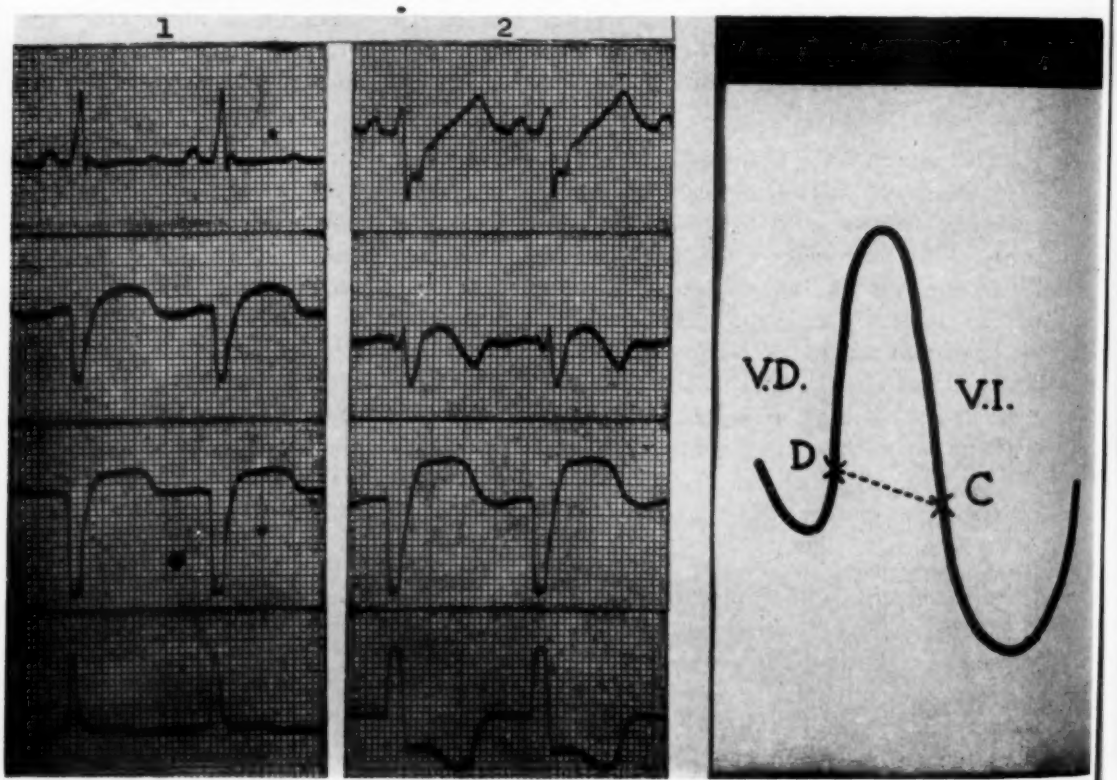


Fig. 2.—Bipolar transeptal lead and unipolar leads from point *C* on the left septal surface, and *D* on the right septal surface, at the levels indicated in the attached schematic. Column *1*, Control tracings: Lead II (first tracing) registered simultaneously with unipolar leads from the points *D* (second tracing) and *C* (third tracing) and with the bipolar transeptal lead taken between *C* and *D* (fourth tracing). *2*, The same leads as in Column *1* after producing right bundle branch block.

II and from 0.015 to 0.02 second before the vertex of the bipolar Lead C′-D′. In addition, the vertex of the bipolar Lead C-D is synchronous with the middle portion of the ascending limb of R in standard Lead II, and the vertex of bipolar Lead C′-D′ is synchronous with the beginning of the descending limb of R in this same lead. The rapid complex of the two bipolar leads is positive, which suggests that at both levels activation takes place from left to right. The sequence of activation recorded by the bipolar leads is due to the fact, already pointed out, that the septal activation occurs earlier in the lower portion than in the upper.

In Columns 2, 3, and 4 are shown the same leads as in Column 1, but with increasing grades of right bundle branch block. In Column 2, with very slight degree of block, both bipolar leads show increased duration of QRS and a plateau in the superior portion of this complex. The bipolar Lead C-D has a duration of about 0.04 second and the bipolar Lead C′-D′, of about 0.05 second. With an increased degree of block in Column 3, the complexes are slightly wider. In Column 4, with the greatest degree of block obtained, both bipolar leads, especially bipolar Lead C-D, become wider and their plateaus show increased duration.

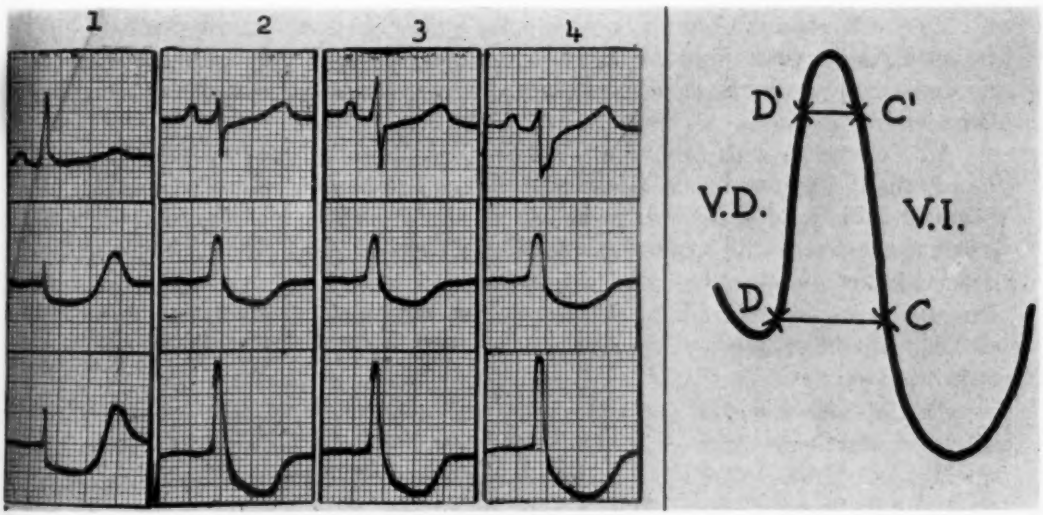


Fig. 3.—Bipolar transeptal leads registered between the points indicated in the attached drawing. *1*, Control tracings: Lead II (upper tracing) registered simultaneously with the bipolar transeptal lead between the points *C* and *D* (middle tracing) and the bipolar transeptal lead between the points *C′* and *D′* (lower tracing). *2* to *4*, The same leads as in *1*, but with increasing degrees of right bundle branch block.

With right bundle branch block, activation at both levels continues to take place from left to right, but it is interesting to note that a distinct difference exists between the bipolar tracing of control (Column 1) and those corresponding to a slight degree of block (Column 2). In the later, there appears a frank plateau that was not present in the control. The presence of the plateau and the greater duration of these bipolar leads suggest that even with slight grades of block there occurs an important delay of activation between the two septal surfaces, a delay which, according to what we have pointed out in experiments such as those shown in Fig. 1, is not caused by the left ventricular septal mass. In the tracings of

Columns 3 and 4, with greater degree of block, the differences from the tracings of incomplete block of Column 2 are minor, and are manifested solely by greater duration of QRS and accentuation of the plateau.

D. The fact that, with right bundle branch block, delay of conduction was not present in the left ventricular muscle but was, on the other hand, quite significant between the two septal surfaces suggested a study using bipolar leads between two septal points very close together; one point being activated by one bundle branch and the other point activated by the other branch. Figs. 4 and 5 illustrate typical tracings obtained in this study.

In the experiment corresponding to Fig. 4, two septal points very close together were explored, point *D* on the right septal surface and point *C*, 2 mm. below within the septum.

In Columns 1 to 7 of Fig. 4, standard Lead II is shown (upper tracing), taken simultaneously with the bipolar lead between points *C* and *D*. In Column 1 the control tracing is shown and, in the subsequent columns, tracings taken with increasing grades of right bundle branch block. The connections were made in such a way that positivity in the bipolar tracing indicated that the wave of activation reached point *C* first.

As can be seen in Column 1, the bipolar Lead C-D is essentially positive and its vertex is inscribed approximately 0.0225 second after the beginning of QRS in Lead II, and is synchronous with the middle portion of the upstroke of R in the same lead.

In Column 2, with minimum grade of right bundle branch block, in spite of only slight modifications of QRS in Lead II, it can be seen that the bipolar lead is considerably modified: it is widened and shows a plateau whose final portion is synchronous with the beginning of the downstroke of S in Lead II. The bipolar Lead C-D in Columns 2 to 7 shows progressive increase in duration. In Column 7, with the maximum grade of block obtained, the bipolar leads have a duration of 0.045 to 0.05 second and the final portion is synchronous with the notch of S in Lead II.

In Columns 8 and 9, Lead II (uppermost tracing) recorded simultaneously with unipolar leads from point *D* (middle tracing) and from point *C* (lowest tracing) are shown. Column 8 is a control tracing and Column 9 shows complete right bundle branch block. The intrinsic deflection of the unipolar lead at point *C* in the control tracing is inscribed 0.015 second after the beginning of QRS in Lead II and is registered 0.0025 second before the vertex of the intrinsic deflection of the unipolar lead at point *D*. With complete right bundle branch block, it is seen that unipolar Lead C continues to be recorded early and is not fundamentally modified, while the unipolar Lead D acquires an RS morphology, and the vertex of its intrinsic deflection is registered about 0.04 second later than that of the unipolar Lead C. These changes clearly demonstrate that the activation at point *D* depends on the right bundle branch while the activation at point *C* comes from the left bundle branch.

It is interesting to observe the marked change that takes place in the bipolar Lead C-D between the control tracing and that minimum right bundle branch block. This suggests that, with barely perceptible grades of block in the periph-

eral lead, there exists an important delay between the points *C* and *D*, which increases progressively with increasing grades of block.

This experiment strongly supports the idea that the delay in the wave of activation in right bundle branch occurs in the septum, in a very limited zone, and in this case between the electrodes *C* and *D*.

The unipolar leads clearly show that these two points were activated by different bundle branches, which explains why the bipolar Lead C-D behaves as a bipolar transeptal lead, even though the distance which separates the two electrodes is very slight.

Fig. 5 represents an experiment in which three zones of the right septal surface were explored (*D*, *E*, and *F*). Electrode D was near the base of the anterior papillary muscle, electrode E was less than 1 cm. from point *D*, and electrode F explored a part situated 1.5 cm. from point *E*.

In Column 1 standard Lead II of control (uppermost tracing) is shown simultaneously with unipolar leads from points *D* and *E* (second and third tracings) and a bipolar lead between the points *D* and *E* (fourth tracing). The vertex of the intrinsic deflection of the tracings D and E are practically simultaneous, and the bipolar Lead D-E is positive, which, with this type of connections, indicates that the wave of activation is directed from *D* toward *E*. The vertex of this bipolar lead is inscribed 0.015 second after the beginning of QRS in Lead II. The unipolar lead from point *F*, under control conditions, is similar in time and morphology to that from point *E*, and the bipolar Lead D-F shows the same characteristics as Lead D-E.

In Column 2 the same leads as in Column 1 after the production of right bundle branch block are shown. The unipolar leads from points *D* and *E* show an RS type complex. The intrinsic deflection from point *D* is recorded at 0.05 minute, and that of point *E* at 0.06 second after the beginning of QRS in Lead II, demonstrating that both points depend for their activation, under control conditions, on the right bundle branch. The bipolar lead demonstrates some extrinsic phenomena in its initial part but the intrinsic phenomena continue to be essentially positive and with a morphology similar to that of the control, indicating that the process of activation continues to be carried out from below upward. The vertex of the maximum deflection of the bipolar Lead D-E is inscribed 0.045 to 0.05 minute after the beginning of QRS in Lead II, and is synchronous with the inferior vertex of the intrinsic deflection of unipolar Lead E, and with the most slurred portion of the downstroke of S in Lead II.

In Column 3 Lead II with right bundle branch block (upper tracing) simultaneously with unipolar leads from points *D* (second tracing) and *F* (third tracing) and with the bipolar Lead D-F (fourth tracing) is shown. Unipolar Lead D is analogous to that described in Column 2, while unipolar Lead F is essentially negative and its intrinsic deflection is not retarded (it is inscribed about 0.015 second after the beginning of QRS in Lead II) which suggests that the activation at point F is carried out by the left bundle branch also. It is interesting to note that, when right bundle branch block is produced, there is a difference of 0.03 second between the intrinsic deflections of the points *E* (Column 2, third tracing) and *F* (Column 3, third tracing), which are situated very close to each other, a

distance of 1.5 mm. The activation of these two points are simultaneous in the control tracings.

The foregoing again supports the conclusion that, when right bundle branch is produced, the delay in conduction occurs precisely in a narrow zone in the site where the wave of activation passes from the regions activated by the intact branch to those which are activated by the blocked branch. The foregoing experiment also suggests that the sequence of ventricular activation in the part of the right septal surface made up by the right ventricle is not modified when right bundle branch block is produced.

2. *Left Bundle Branch Block.*—

A. Using a method similar to that already outlined for right bundle branch block, a study was made, in the first group of experiments, of the modifications that different degrees of left bundle branch block produce in the propagation of the wave of activation in the septal mass of the left ventricle. Fig. 6 illustrates this type of experiment.

In this experiment (Fig. 6), explorations of four points activated by the left branch of the bundle of His were made, points *A* and *B* being situated in the lowest part of the interventricular septum, and points *A′* and *B′* in the upper third of the septum.

In Column 1 the bipolar leads between the points *A* and *B* (middle tracing) and between the points *A′* and *B′* (lowest tracing) simultaneously with standard Lead II as control (uppermost tracing) are shown. Both unipolar leads are predominantly positive, indicating that the path followed by the wave of activation at those levels is from left to right. The vertex of the positive deflection of the bipolar Lead A-B is inscribed approximately 0.005 second after the beginning of QRS in Lead II and falls about 0.0125 second before the vertex of the positive deflection of the bipolar Lead A′-B′. These relationships indicate that the zones situated at the level *A-B* are activated before those located at *A′-B′*.

In Columns 2 to 9 the same leads as in Column 1, with increasing grades of left bundle branch block, are shown. Bipolar Lead A-B with a minimal degree of block (Columns 2 to 5) shows some delay with respect to the control, but its morphology does not vary. Beginning in Column 6 there appears a slight slurring that is converted later into a small positive deflection. The principal deflection continues to be positive, with the same morphology as the control, and its vertex, when the block is complete (Column 9), is inscribed 0.05 second after the beginning of QRS in Lead II; that is, the activation between the points *A* and *B*, with the greatest degree of block obtained, even though considerably retarded, is not changed in direction.

Bipolar Lead A′-B′ behaves as this type of lead between two left septal points has been habitually observed to behave. With a minimal degree of block (Columns 2 to 5), it continues to be positive and its vertex is increasingly delayed with respect to the control. It shows, moreover, a small notch in the downstroke of R. With the greater degree of block in Column 6, the bipolar lead is inverted, indicating that the activation at this time goes from *B′* toward *A′*. In Columns 6 to 9, the bipolar Lead A′-B′ continues to be inverted, the principal deflection (Column 9) showing a slight increase in duration without marked widening.

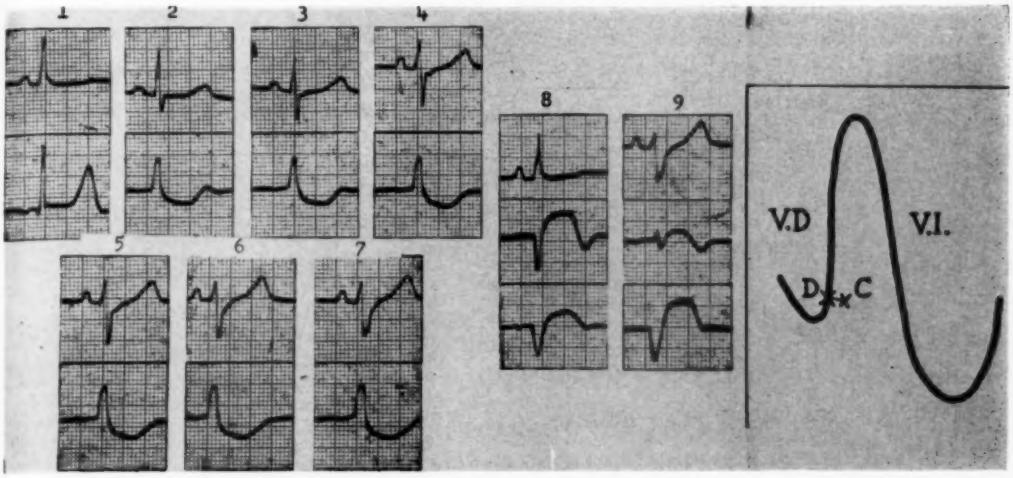


Fig. 4.—Close bipolar lead and unipolar leads corresponding to the sites illustrated in the adjoining drawing. *1*, Control tracings: Lead II (upper tracing) registered simultaneously with the bipolar lead between the points *C* and *D*. The connections of the bipolar Lead C-D were made in such a way that a positive deflection in the bipolar tracing implies that the wave of activation reaches the electrode C before it reaches D. *2* to *7*, The same leads as in *1*, but with increasing degrees of right bundle branch block. *8* and *9*, Lead II (upper tracing) taken simultaneously with unipolar leads from the points *D* (middle tracing) and *C* (lower tracing); control tracings in *8* and with right bundle branch block in *9*.

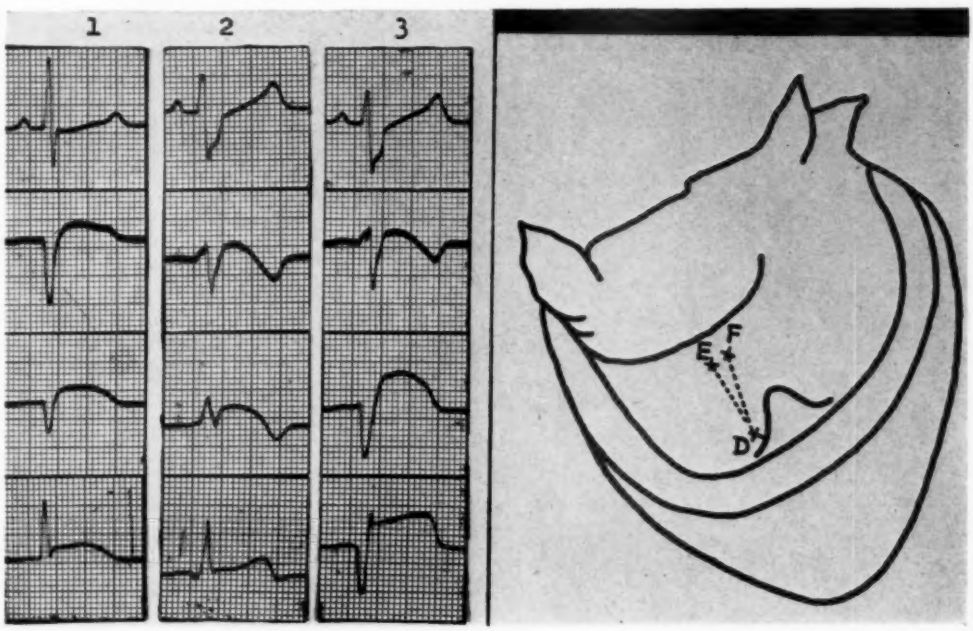


Fig. 5.—Bipolar lead and unipolar leads registered on the right septal surface in the manner illustrated in the adjoining schematic. Electrode D was situated close to the base of the anterior papillary muscle and electrode E at less than 1 cm. from electrode D. Electrode F explored a region located 1.5 mm. from point *E*. *1*, Control tracings: Lead II (first tracing) registered simultaneously with the unipolar leads from point *D* (second tracing) and from point *E* (third tracing) and with the bipolar lead between *D* and *E* (fourth tracing). The positive deflection of the bipolar Lead D-E, with our type of connections, indicates that the wave of activation is directed from *D* to *E*. *2*, The same leads as in *1* after the production of right bundle branch block. *3*, Lead II (first tracing) simultaneous with the unipolar leads from the points *D* (second tracing) and *F* (third tracing) and with the bipolar lead between *D* and *F*, with right bundle branch block.

With the greatest degree of block obtained, the inferior vertex of the negative deflection of the bipolar Lead A′-B′ is inscribed from 0.0375 to 0.04 second after the beginning of QRS in Lead II, and 0.01 minute before the vertex of the positive deflection of the bipolar Lead A-B.

The fact that inversion of the bipolar Lead A-B is not observed, even with complete block, is explained by the location of the electrodes in the very low portions of the septum. It is very probable that after the production of block, the tissue at electrode A continues to be activated before that at electrode B.

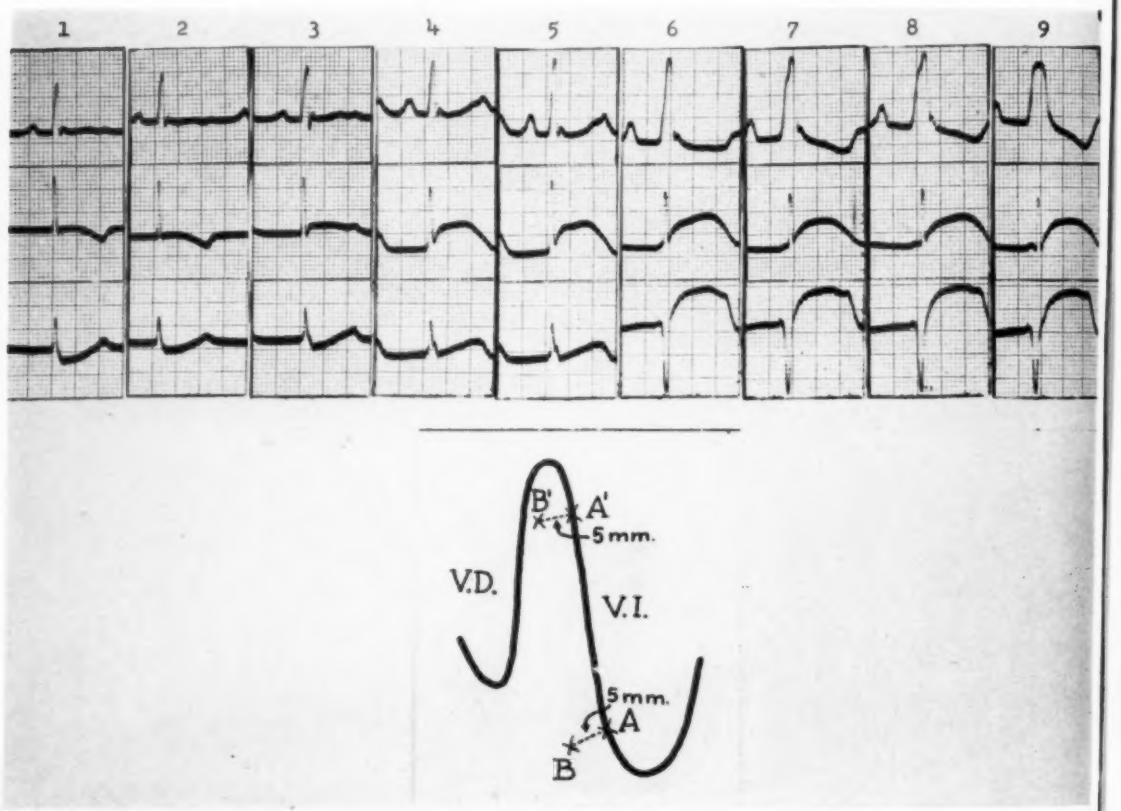


Fig. 6.—Bipolar leads registered between the four left septal points indicated in the attached schematic. Note that the distance between the sites *A* and *B*, and between *A′* and *B′*, is about 5 mm. *1*, Control tracings: Lead II (upper tracing) recorded simultaneously with bipolar leads between the points *A* and *B* (middle tracing) and between the points *A′* and *B′* (lower tracing). *2* to *9*, The same leads as in *1*, but with increasing degrees of left bundle branch block.

The initial positive deflection, apparently extrinsic, that precedes the principal deflection of the bipolar Lead A-B in the last four columns, and which also is seen to precede the principal deflection of the bipolar Lead A′-B′, would seem to correspond to the moment in which there occurs the passage of the wave of activation from the portions activated by the right branch to those which before were activated by the left branch, since it is synchronous with the upstroke of R in Lead II.

It is interesting to observe that activation is retarded in different ways at different levels of the septum. For example, the inferior zones *A-B*, which in controlled conditions were activated before the superior zones *A'-B'*, are activated later when significant degrees of left bundle branch block are produced.

In bipolar leads registered between two points 5 mm. apart (Fig. 6) and even farther apart, the point from which the records are taken depend for their activation on the left bundle branch. It is seen that these bipolar tracings do not become significantly widened when block is produced. This suggests that, in spite of the fact that the direction of activation is reversed with left bundle branch block, significant delays in the propagation of the wave of activation between regions corresponding to left septal muscle do not exist, even when, in general, activation of all the left septal mass is retarded.

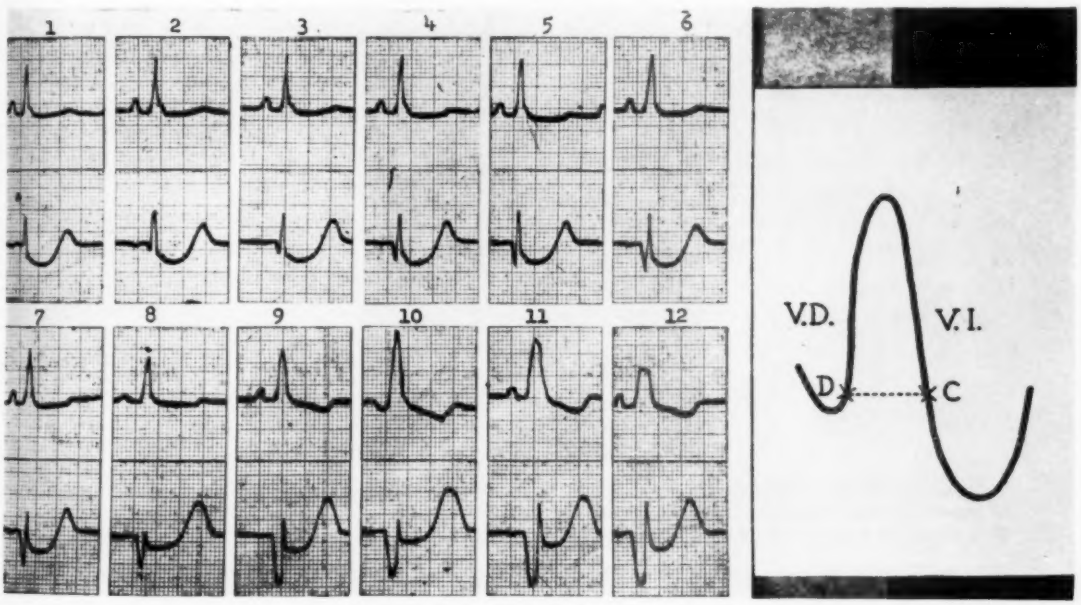


Fig. 7.—Bipolar transeptal lead between the point *C*, on the left septal surface, and *D*, on the right septal surface, at the level shown in the adjoining drawing. *1*, Control tracings: Lead II (upper tracing) simultaneous with the bipolar transeptal lead between *C* and *D* (lower tracing). *2* to *12*, The same leads as in *1* but with increasing degrees of left bundle branch block.

B. In a second group of experiments, the changes produced by bipolar transeptal leads were studied. In the experiment shown in Fig. 7, a bipolar transeptal lead (lower tracing) was recorded between a left septal point, *C*, and a right septal point, *D*, the latter dependent on the right bundle branch for its activation. The transeptal lead was taken simultaneously with Lead II (upper tracing). The control leads are shown in Column 1, and it can be seen that the transeptal tracing is entirely positive and its vertex is inscribed about 0.02 second after the beginning of QRS in Lead II. This positive deflection indicates that the process of activation is carried out, at this level, from left to right.

In the remaining columns (2 to 12) the same leads as in Column 1, but with increasing grades of left bundle branch block, are shown. It is pointed out that in the bipolar transeptal lead of Column 2, with a slight degree of left bundle branch block, the appearance of a small negative initial deflection (Q wave) begins to be recorded before the QRS in Lead II, the vertex of which is synchronous with the beginning of QRS in the same lead. As the degree of block increases (Columns 2 to 7), the Q wave increases in voltage as well as duration, while the R wave diminishes, the two waves finally becoming approximately equal in Columns 6 and 7. The beginning of the Q wave continues to precede the beginning of QRS in Lead II and the vertex of Q is progressively delayed until in Column 7 it is registered 0.02 second after the beginning of QRS in Lead II. In Column 8, the Q wave is greater than the R wave, and its vertex is recorded 0.035 second after the beginning of QRS in Lead II. Beginning with Column 9, the Q wave becomes even more widened, and a plateau is seen in its lower portion.

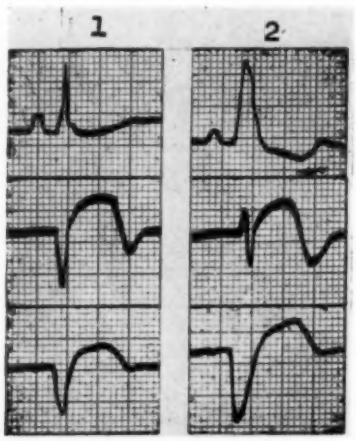


Fig. 8.—Unipolar leads corresponding to the experiment of Fig. 7. *1*, Control tracing: Lead II (upper tracing) registered simultaneously with unipolar leads from the point *C* (middle tracing) and from the point *D* (lower tracing). *2*, The same leads as in *1* but with left bundle branch block.

The downstroke is registered 0.01 second before the beginning of the ventricular complex in Lead II. The R wave is progressively delayed, which can be easily appreciated when it is compared to the vertex of R in Lead II. In Columns 1 to 7, the vertex of the positive deflection of the bipolar transeptal lead precedes the vertex of R in Lead II. In Column 8, these vertexes are approximately synchronous, and in the last four columns, the vertex of the bipolar lead is recorded after that of Lead II. This positive deflection persists even with the maximum degree of block produced (Column 12); its vertex being recorded 0.05 second after the beginning of QRS in Lead II.

In Fig. 8, the unipolar leads corresponding to the last experiment are shown. In each column there is a standard Lead II (uppermost tracing) taken simultaneously with the unipolar leads from the left septal point (middle tracing) and from the right septal point (lowest tracing). In the control tracings (Column 1), the vertex of the unipolar record from left septal point *C* is registered 0.02 second after the beginning of QRS in Lead II and that of the right septal tracing *D* from 0.025 to 0.03 second after the beginning of QRS in the same lead. With

left bundle branch block (Column 2) there is no delay at right septal point *D*, while there is at the left septal point *C*, it being inscribed 0.05 second after the beginning of QRS in Lead II.

It is interesting to observe the relationship between the times of inscription of the unipolar leads at each of the two septal points in Fig. 7. When left bundle branch block is produced, the first downstroke of the bipolar transeptal lead (Column 12, Fig. 7) is inscribed at the same time as the intrinsic deflection of the right septal portions normally activating the right bundle branch. The vertex of the R wave, which persists with the maximum degree of block obtained (Column 12, Fig. 7), is inscribed at the same time as the inferior vertex of the intrinsic deflection of the left septal unipolar lead (Column 2, Fig. 8) and it corresponds, in all probability, to the portions of the left septal surface at which there is the greatest delay.

As we have already pointed out, with the polarity of the connections that were used in these studies, an essentially positive ventricular complex from the bipolar lead indicates that the general direction of the process of activation at this level is from left to right. Therefore, the appearance of a negative initial component suggests that, at the beginning of the process of activation, forces have been produced which are developed in the opposite direction, that is, from right to left. This negative component increases in voltage and duration proportionately with the increase in degree of block. This implies that, with the increase in the conduction disturbance, the septal forces being developed in reverse direction acquire greater importance. The rather abrupt change observed in the negative deflection of the bipolar transeptal lead from Column 8 to Column 9 is striking. The appearance of a frank plateau that did not exist in the previous tracing (Columns 2 to 8) suggest that, with the degree of block seen in Column 9, there occurs a marked delay in the wave of activation when it passes from right to left.

In the experiment illustrated in Fig. 9, two septal points were explored, point *C* on the left septal surface and point *D* on the right septal surface. In Column 1 is shown standard Lead II (first tracing), taken simultaneously with the unipolar leads of the points *C* and *D* (second and third tracing, respectively) and with the bipolar lead between *C* and *D* (fourth tracing). The inferior vertex of the intrinsic deflection of point *C* is recorded approximately 0.0125 second after the beginning of QRS in Lead II and 0.005 second before the inferior vertex of the intrinsic deflection of point *D*, which is to say that point *C* is activated before point *D*, but with very slight differences in time. Bipolar Lead C-D is positive, indicating that the direction of activation at this level is from left to right. The superior vertex of the rapid complex of the bipolar lead is registered about 0.005 second after the beginning of QRS in Lead II. It can be seen that the superior vertex of the bipolar leads is inscribed as a small plateau.

With left bundle branch block, shown in Column 2, the unipolar lead from point *D* (third tracing), which depends for its activation on the right branch, becomes entirely negative and increases in duration. The intrinsic deflection of this lead continues to be inscribed without delay. The inferior vertex of the intrinsic deflection of unipolar lead (second tracing) is inscribed about 0.08

second after the beginning of QRS in Lead II and 0.06 second after the vertex of the intrinsic deflection on the right septal unipolar lead at point *D* (third tracing).

The bipolar Lead C-D in left bundle branch block is inverted, and shows a plateau of about 0.04 second duration and a late positive deflection the vertex of which is inscribed 0.08 second after the beginning of QRS, and is synchronous with the vertex of the intrinsic deflection of the left septal unipolar lead at point *D*.

The time relationship between the unipolar leads of each of the septal points and of the bipolar transeptal lead are similar to those described in the experiment illustrated by Figs. 7 and 8 and need not be noted again.

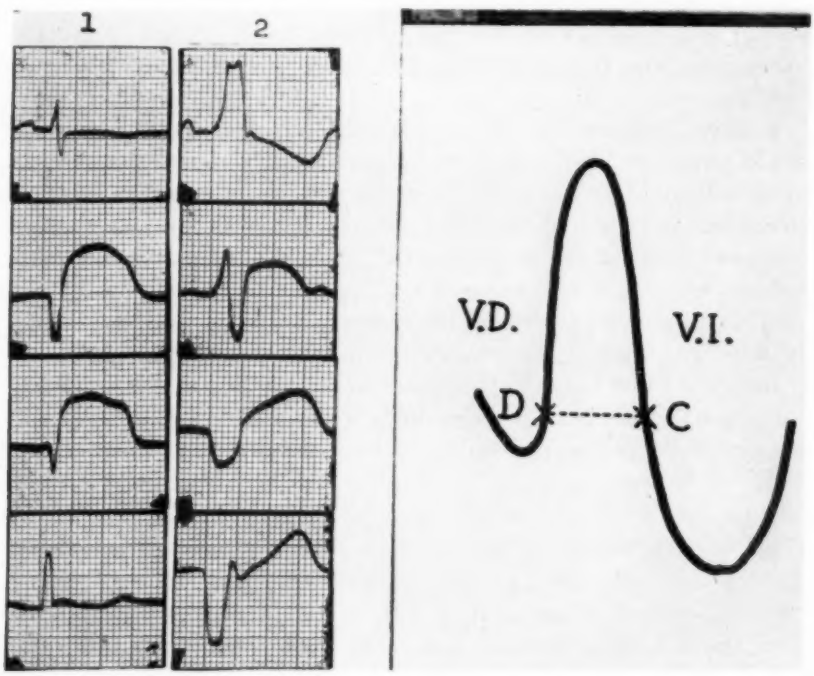


Fig. 9.—Bipolar transeptal lead and unipolar leads registered at the points *C* and *D*; *D* from the right septal surface and *C* from the left, at the level shown in the adjoining schematic. *1*, Control tracings: Lead II (first tracing) simultaneous with unipolar leads from the point *C* (second tracing) and *D* (third tracing) and with the bipolar lead between *C* and *D* (fourth tracing). *2*, The same leads as in *1* after producing left bundle branch block. Note the persistence of the delayed positive deflection in the transeptal Lead C-D, with the maximum degree of block obtained. This is also seen in the experiment of Fig. 8.

The principal negative deflection of the bipolar Lead C-D in left bundle branch block results from the reversal of direction of the process of activation, which now takes place, in general, from right to left. Moreover, the presence of a plateau of marked duration is evidence that the wave of activation underwent a delay passing from the regions activated by the conducting branch to those which are now blocked. This delay, as was pointed out in Section A, does not exist in the bipolar tracings taken between left septal points, notwithstanding the distance between them and even the great degree of block. The late positive deflection of the transeptal bipolar lead persists with the greatest degree of left bundle branch block obtained in experiments such as those illustrated by the Figs. 7 and 9. This suggests the existence of regions which, although greatly delayed in their activation, continue to be activated through the left bundle branch.

C. Because of the persistence of a late positivity in the bipolar tracings (Figs. 7 to 9), a study was made to ascertain if the total section determines completely negative bipolar transeptal tracing.

Fig. 10 shows Lead II (uppermost tracing) with complete left bundle branch block (the greatest degree obtained after a wide section of the left bundle branch), simultaneously with the bipolar transeptal Lead C-D (middle tracing), recorded at the level of the inferior third of the septum, and Lead C′-D′ (lowest tracing) obtained at the superior third of the septum. Both bipolar leads are of marked duration, essentially negative, and it is noted that the bipolar Lead C′-D′ does not show a late positive deflection, which suggests that under these conditions and at this level (Lead C′-D′), activation takes place completely from right to left.

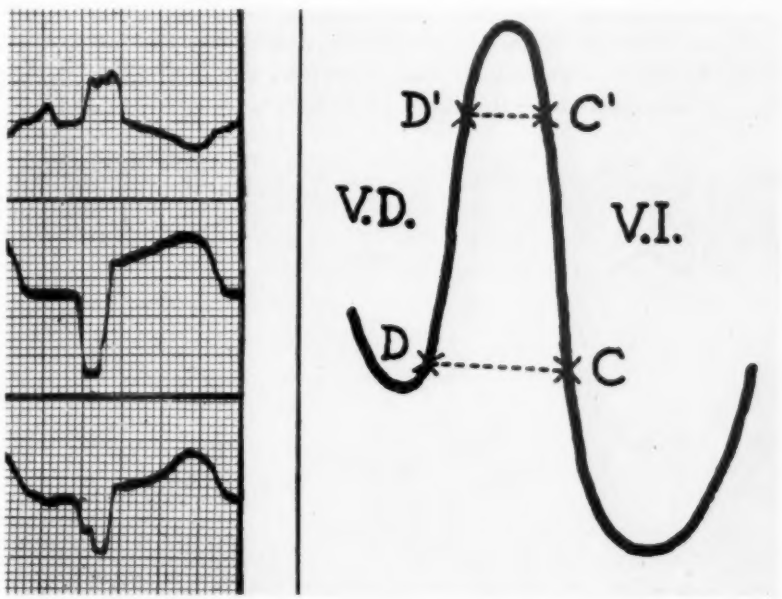


Fig. 10.—Bipolar transeptal leads at the levels indicated in the adjoining drawing after sectioning the left bundle branch widely and deeply. Lead II (upper tracing) simultaneous with the bipolar transeptal between *C* and *D* (middle tracing) and the bipolar transeptal between *C′* and *D′* (lower tracing).

In the lower bipolar tracing, Lead C-D, a small but definite persistent positive deflection is again seen. In the majority of the experiments of this type, the late positive deflection does not appear in the bipolar transeptal leads recorded at high levels, but persists, although of small magnitude, in the same leads taken at lower levels.

The foregoing experiment demonstrates that it is possible to obtain, with complete left bundle branch block, negative transeptal tracings (lowest tracing, Fig. 10). Nevertheless, even in this experiment there was a late positivity in the lower transeptal tracing. In an attempt to explain the mechanism of production of this delayed positive deflection the following possibilities are suggested:

1. Notwithstanding the fact that an effort was made to section completely the left bundle branch, it is possible that some fibers remained and a certain degree of conduction through the bundle persisted.

2. The muscular portions of the septum adjacent to the surface may not be activated simultaneously, which might cause final activation to take place from below upward and from left to right.

3. In the lower levels of the septum and in areas near the apex of the heart, it appears that the process of the activation of the corresponding muscular mass continues to take place from left to right (Fig. 6). This process is manifested only when all the forces moving in the opposite direction as a result of the block have disappeared.

4. Finally, in this type of experiment we cannot discard the possibility that injured tissue is capable of producing a late positivity.

D. As has been already pointed out in Sections A and B, left bundle branch block does not cause important delays between points activated by the left bundle branch, but does cause significant differences between the two septal surfaces. In order to determine more precisely at what point the delay occurs, and to compare the effects that the block has on the bipolar transeptal leads and on the bipolar leads between relatively distant points on the left septal mass, studies similar to those illustrated by the Figs. 11 and 12 were carried out.

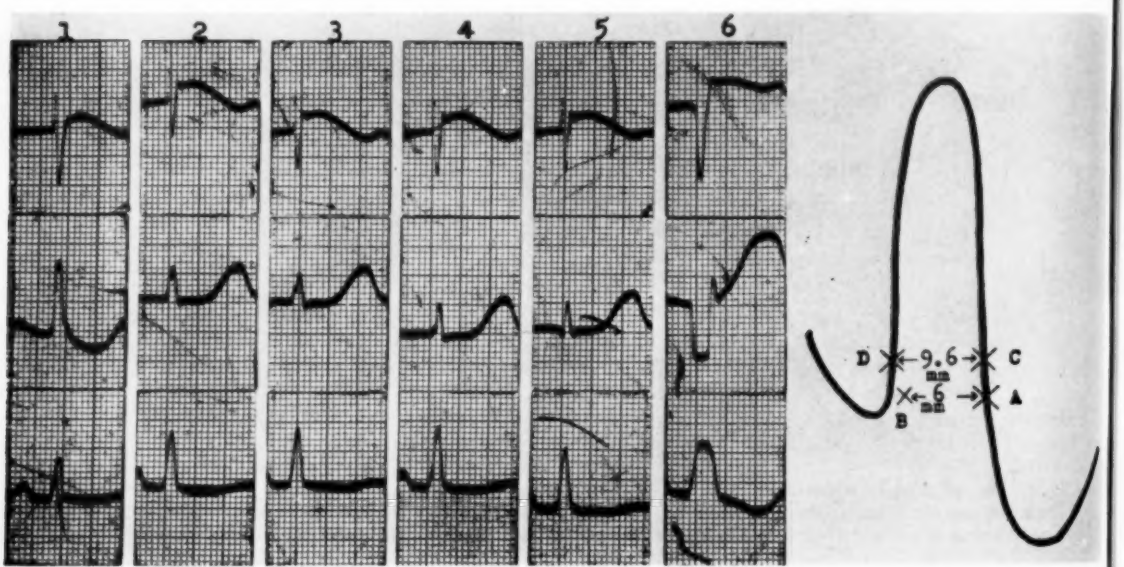


Fig. 11.—Bipolar lead between left septal points, and bipolar transeptal lead registered between the zones illustrated in the adjoining schema. Points *A* and *B* are 6 mm. apart and the points *C* and *D* are 9.6 mm. apart. *1*, Control tracings: bipolar lead between the points *A* and *B* (upper tracing), registered simultaneously with the bipolar transeptal lead between the points *C* and *D* (middle tracing) and with Lead II (lower tracing). *2* to *6*, The same leads as in *1* but with increasing degrees of left bundle branch block.

Fig. 11 shows bipolar leads registered at the points indicated in the adjoined schema. In Column 1 is shown standard Lead II (lower tracing) taken simultaneously with a bipolar lead from the two septal points *A* and *B* located in the left septal mass at a distance of 6 mm. from each other (upper tracing) and with a bipolar transeptal lead between a left septal point *C* and a right septal point *D* (middle tracing).

The bipolar Lead A-B between the left septal points shows an RS morphology, and has a very rapid inscription. The vertex of R precedes the beginning of QRS

in Lead II by 0.01 second, while the vertex of S is synchronous with the beginning of QRS in the same lead. Bipolar transeptal Lead C-D is positive and the direction of activation is from *C* to *D*. This bipolar lead begins to be registered before the beginning of QRS in Lead II, but its inscription is not as rapid as that of the bipolar Lead A-B. Moreover, a slight plateau is seen whose initial part is synchronous with the beginning of QRS in Lead II.

In the subsequent columns (Columns 2 to 6) are shown the same leads as in Column 1, but with increasing grades of left bundle branch. The bipolar lead shows a slight but progressive delay in inscription as the grade of block increases, but continues to be inscribed rapidly and maintains the morphology RS up to Column 5. In Column 6, with the maximum degree of block attained, bipolar Lead A-B becomes inverted and the vertex of its negative deflection is inscribed from 0.035 to 0.04 second after the beginning of QRS in Lead II. These changes which are observed in the bipolar Lead A-B indicate that with minor degrees of left bundle branch block there is progressive delay in the arrival of the wave of activation at left septal points, but the direction of activation is not changed. With complete block, the direction of activation is reversed, taking place from *B* to *A*, but it is interesting to note that its inscription remains relatively rapid, although of slightly greater duration than is found when activation takes place in a normal direction.

On the other hand, the bipolar transeptal lead behaves in quite a different manner. With a minimal degree of block as seen in Column 2 it shows a small notch in the superior portion of the ascending limb of R and the vertex of R is inscribed 0.035 second after the beginning of QRS in Lead II. As the grade of block increases, the above-mentioned notch begins to descend, being found in the middle part of the ascending limb of R in Column 3 and in the initial part of the upstroke of R in Column 4. In Column 5, with a still greater degree of block, this notch is replaced by an initial negativity whose vertex is inscribed 0.02 second after the beginning of QRS in Lead II, while the vertex of R in the same lead is registered from 0.0175 to 0.02 second later. In Column 6, with the maximal degree of block, the bipolar transeptal lead becomes inverted and is essentially negative. The negative component is of considerable duration, the beginning of its downstroke coinciding with the beginning of QRS in Lead II and the final vertex of the descending limb is registered from 0.015 to 0.0175 second later, following which there is a plateau of 0.045 second's duration.

The fact that the notch in the bipolar transeptal lead occurs progressively earlier in the complex as the degree of block increases, and that this notch is synchronous with the S wave of the bipolar Lead A-B, suggests that it is related to activation of right ventricular portions of the septum. When the greatest degree of block is attained, the negative deflection which replaces the notch is also synchronous with the S wave of the bipolar Lead A-B, which suggests that now the first forces of activation correspond to those of the right ventricle. Therefore, if we refer the ascending limb of R of the bipolar transeptal Lead C-D to left septal forces, it must be pointed out that, when the notch is produced, there are developed at the same time and, in the reverse direction, right septal forces. All the foregoing suggest that this notch is the result of forces that are

developed in reverse direction, that is, those originating on the right septal surface, from right to left, and those originating on the left, from left to right.

The descent of the notch which is seen in Columns 3 and 4 would correspond, then, to a progressively earlier manifestation of the right septal forces, parrallel to the increasing delay in the left septal regions. The negative deflection that replaces the notch in Column 5 can be interpreted as showing that activation of the right septal point precedes the left, even when activation of the left septum, already retarded, continues to be carried out by the left bundle branch and, in general terms, from left to right.

The negative deflection of the bipolar transeptal Lead C-D in Column 6 indicates that, at this moment, activation takes place from right to left. However, the presence of a greatly widened plateau complex in this lead, totally different from the complexes registered between the left septal points, suggests that there has occurred a marked delay in the wave of activation at the moment in which the wave passes from the portions activated by the right branch to those normally corresponding to the left branch. It is not likely that this plateau represents an equally slow propagation of the wave of activation along the mass of the septum. Such an idea is opposed by the fact that activation takes place relatively rapidly between the points *A* and *B*, 6 mm. apart. The principal delay occurs in a zone situated approximately between the regions explored by points *B* and *D*, that is, in a relatively small area which we have calculated in this experiment to be less than 3 mm.

In Fig. 12, unipolar leads from the previous experiment are shown. In Columns 1 and 2 are shown standard Lead II (upper tracing) taken simultaneously with unipolar leads from point *A* (middle tracing) and point *B* (lower tracing). Column 1 shows a tracing taken in controlled conditions and in Column 2 there is complete left bundle branch block. The vertex of the intrinsic deflection of the unipolar Leads A and B in the control are practically simultaneous and are registered approximately 0.01 second or less after the beginning of QRS in Lead II. With complete left bundle branch block, the vertex of the intrinsic deflection of the unipolar septal Lead A (before the slurring) is inscribed 0.06 second after the beginning of QRS in Lead II and comes after the inferior vertex of the intrinsic deflection of the unipolar Lead B by about 0.0175 to 0.02 second. That is to say, point *B* located in the thickness of the septal muscle is activated before point *A*, which is consistent with the inversion of the bipolar Lead A-B of Column 6, (Fig. 11) indicating that, under these conditions, activation takes place from right to left. Between both points there now exists a certain degree of delay in the propagation of the wave of activation. The difference of approximately 0.0175 to 0.02 second between the activation of the points *A* and *B* (in the bipolar as well as the unipolar leads) corresponds to a velocity of conduction of approximately 352 mm. per second.

In Columns 3 and 4, Lead II (upper tracing) taken simultaneously with unipolar lead at points *C* (middle tracing) and *D* (lower tracing) is shown. Column 3 is under control conditions, and Column 4 with complete left bundle branch block. In the control tracings, it is seen that the vertex of the intrinsic deflection of unipolar Lead C is inscribed approximately 0.005 to 0.01 second

after the beginning of QRS in Lead II and precedes the vertex of the intrinsic deflection of unipolar Lead D by 0.02 to 0.025 second. With complete left bundle branch block, as shown in Column 4, the left septal unipolar lead (middle tracing) shows considerable delay and the vertex of its intrinsic deflection is inscribed

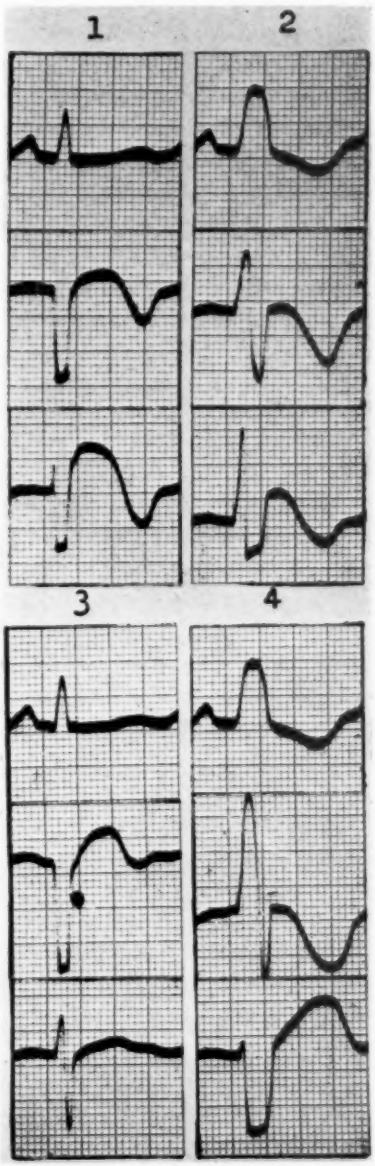


Fig. 12.—Unipolar leads corresponding to the same sites explored in the experiment of Fig. 11: *A* and *C* on the left septal surface, *D* on the right septal surface, and *B* in the substance of the interventricular septum. *1*, Control tracings: Lead II (upper tracing) simultaneous with unipolar leads from point *A* (middle tracing) and from point *B* (lower tracing). *2*, The same leads as in *1* but with the maximum degree of left bundle branch block obtained. *3*, Control tracings: Lead II (upper tracing) simultaneous with unipolar leads from point *C* (middle tracing) and from point *D* (lower tracing). *4*, The same leads as in *3* but with left bundle branch block.

about 0.07 second after the beginning of QRS in Lead II. The right septal unipolar lead (lower tracing) is essentially negative. Its positivity diminishes with respect to the control, and the inferior vertex of its intrinsic deflection is inscribed 0.025 second after the beginning of QRS in Lead II and, consequently, 0.05 second before that of the unipolar Lead C.

Between both septal surfaces (*C* and *D*), 9.6 mm. apart, there is a difference of 0.05 second in the times of arrival of the wave of activation. Nevertheless, their relationship under control conditions showed that point *C* is activated 0.02 second before point *D*, for which reason the true delay at *C* caused by the block is actually 0.07 second. The left septal points *A* and *B*, 6 mm. apart, show a difference of only 0.0175 to 0.02 second. This permits the conclusion, as was already suggested by the bipolar transeptal lead, that between the points *B* and *D*, being only 3.6 mm. apart although being activated by different bundle branches under control conditions, there is an important difference between the times of arrival of the wave of activation when left bundle branch block is produced.

DISCUSSION

The interventricular septum was explored electrocardiographically using both proximal and distant bipolar leads at different septal levels, and under controlled conditions as well as with varying degrees of bundle branch block.

In a previous publication,[1] in which an incomplete study of septal activation was made, a number of new concepts regarding it were advanced; in this series of experiments we were able to corroborate them and amplify them in a detailed manner.

Under controlled conditions we were able to confirm that septal activation is carried out from left to right at whatever level selected. Our studies have shown repeatedly that the lower portions of the septum are activated earlier than the upper portions.

In the control tracing it was found that in practically all of the mass of the interventricular septum that was formed by the left ventricle the velocity of conduction* fluctuated between 1,000 and 1,200 mm. per second. Therefore, the propagation of the wave of activation in this portion of the septum was exceedingly rapid, approximately 2.5 to 3 times greater than the rate given by Lewis[4,5] for the ventricular muscle and intermediate between values given by the same author for ventricular muscle and the Purkinje network. The figures which we found were closer to those obtained by Erlanger[6] for the Purkinje tissue of the calf (750 mm. per second).

This very rapid speed of conduction in the substance of the septum suggested that the Purkinje fibers penetrate very deeply into the thickness of the interventricular septal musculature.

Numerous workers[7,8,9] have advanced two principal possibilities to explain the widening of the ventricular complex in bundle branch block. First, in bundle branch there is a slow propagation of the wave of activation through the septum;

*It should be pointed out that, in these experiments, the velocity of conduction was measured between two or more points which were to lie in the general direction followed by the impulse.

the wave follows the same pathway but the speed of conduction is diminished. Second, the speed of conduction is the same but the pathway followed is longer, from left to right in right blocks and from right to left in left blocks, accepting the idea of Lewis that the wave of activation under normal conditions invades the septum from both surfaces. This implies that the impulse coming from each branch covers one-half of the thickness of the interventricular septum. In the absence of direct data to support either contention, it is generally accepted that the greater duration of QRS in bundle branch block is due to the time that is needed by the wave of activation to cross the septum and reach the blocked branch below the side of block. The present work yields data that make both of these hypotheses untenable.

In any consideration of bundle branch block, right as well as left, it is well to keep in mind a concept which we have emphasized repeatedly, namely, that by far the greatest part of the interventricular septum is activated by the left branch of the bundle of His. Those portions which depend for their activation on the right branch are limited almost exclusively to the right septal surface, and penetrate hardly at all into the mass of the septum.

1. *Right Bundle Branch Block.*—The various grades of right bundle branch block do not modify the direction or the sequence of the process of activation in the entire left septal mass, in which activation continues to take place, in general, from left to right. The velocity of conduction remains practically the same (from 1,000 to 1,200 mm. per second) even with the greatest degree of right bundle branch block that can be attained. We can conclude that in this type of block there is no modification of the process of activation in the greater part of the interventricular septum, that formed by the left ventricle and activated by the intact left bundle branch.

On the other hand, bipolar transeptal leads (Figs. 2 and 3) demonstrate that in right bundle branch block there are significant differences in the times of arrival of the wave of activation at the two septal surfaces. This difference is about 0.06 second. The direction of activation is not altered, and it continues to be carried out from left to right. If we considered only the bipolar transeptal tracings, it would be reasonable to ask if this delay in conduction were due to a uniformly slow propagation of the wave of activation across the entire septum, or if it occurs in a limited area. The fact that even with the greatest degrees of right bundle branch block there is no conduction delay in entire left septal mass definitely eliminates the former possibility.

With bipolar leads placed so that the distance between the electrodes was increasingly smaller (Figs. 4 and 5) the zone in which the delay occurs in right bundle branch block was precisely localized. It was proved that this delay is about 0.04 second and takes place in a relatively small area (1.5 to 2 mm.), very close to the right septal surface. The delay occurs exactly where the wave of activation passes from regions activated by the left bundle to those which are normally activated by the right bundle.

The mechanism by which this delay takes place is debatable. There are two principal possibilities. First, a change in the speed of propagation as the wave passes from the muscular fibers activated by the left Purkinje system to

the muscular tissue activated by the left Purkinje network. The speed of propagation calculated for this small zone is approximately 37 to 40 mm. per second, an exceedingly low figure, and one which is about one-tenth of that given by Lewis[4,5] for the speed of conduction of the ventricular musculature. No values this low have ever been given for the speed of conduction in the ventricular musculature and it is difficult to give credence to this point of view. Second, the delay may represent a latency in the propagation of the impulse in this zone, which is terminated when the first ramifications of the right Purkinje network are activated. This mechanism might be compared to that observed in the transmission of nerve impulses through synaptic connections. Even though there is no direct and definitive proof of this second possibility, we consider it the more likely in view of the very marked delay occurring in such a small area.

The bipolar transeptal tracings taken at different levels of the septum suggest that the delay caused by right bundle branch block takes place in the lower one-third of the interventricular septum. This is consistent with the fact that activation of the right septal surface normally begins in the lower one-third close to the anterior papillary muscle, and is precisely in this zone where the right bundle branch begins to ramify. This would seem to indicate that the delay in the passage of the wave of activation occurs in those sites where the first ramifications of the right Purkinje network begin, and then all the rest of the right septal surface is activated by the ramifications of the right branch that ascend in this surface. A point in favor of this is the fact that, even when all the right septal surface is significantly delayed in its activation, the sequence in time of arrival of the wave at different points on this surface does not vary.

Up to now, we have discussed right bundle branch block only in terms of maximum degrees of block, which we called complete block. However, between the control tracings and those of complete block there are numerous transitions, the mechanism of which should be considered.

It is noteworthy that while the peripheral leads (Lead II in our experiments) show slight degrees of block, at times difficult to recognize as such (Column 2, Fig. 4), the bipolar transeptal leads, and the close bipolar leads between sites activated by different branches, show considerable widenings that suggest important delays in the process of activation (Figs. 3 and 4). As the degree of block is intensified, the peripheral leads show significant increases in duration and their morphology undergoes change, whereas the above-mentioned bipolar leads increase only in duration (Columns 3 to 7, Fig. 4; Columns 3 and 4, Fig. 3).

In right bundle branch block it is difficult to determine the moment in which the wave of activation begins to pass from the left ventricle to the right ventricle to reach the ramifications of the right Purkinje system. This is because the direction of activation normally and with right bundle branch block is the same, namely, from left to right. The proximal bipolar lead becomes widened with the slightest degrees of right bundle branch block because the wave of activation is retarded along the entire length of the right bundle branch. When this delay is of sufficient magnitude, the stimulus that comes by the left branch "jumps" the physiologic obstacle that is interposed between the two ventricles. It seems that this happens in Columns 6 and 7 of Fig. 4, where Lead II shows marked slurring of the S wave, which is maintained for a considerable period. The

interpretation of these slurrings and their relation to the overcoming of the physiologic obstacle by the wave of activation are easier to evaluate in left blocks (as we shall see later), since in these there is a reversal of the direction of activation when the wave passes from the right ventricle to the left.

The QRS Complex in Lead II in Right Bundle Branch Block.—The findings already pointed out permit us to make certain observations relative to the ventricular complex in Lead II in the presence of right bundle branch block. In the dog, standard Lead II, as well as Leads III and V_F, records variations of potential similar to those recorded from the lateral epicardial surface of the left ventricle. The comments that we will make regarding Lead II are applicable in general terms to leads recording potentials of the lateral surface of the left ventricle. Normally, Lead II shows an essentially positive ventricular complex that may be R, Rs and, at times, qR.

Frequently, under controlled conditions, activation of the interventricular septum is initiated before the ventricular complex in Lead II begins to be inscribed. The Q wave of the left ventricular tracings corresponds to the first septal vector, and represents the vectorial resultant of the activation of the septum from left to right, from the first portions activated on the left side to the base of the anterior papillary muscle, which is the first part activated on the right side. The Q wave corresponds to the first 0.01 second of the septal activation. This first septal vector is manifested in the peripheral lead only when it is oriented in such a manner that it can be projected to the lead considered.

Our septal control tracings suggest that the activation of the septum continues to take place during the first 0.035 to 0.04 second of the inscription of the R wave in Lead II. For this reason, the positive deflection in Lead II that has been attributed mainly to the activation of the free wall of the left ventricle should be considered in the first 0.04 second as the vectorial resultant of septal activation and free left ventricular wall activation.

The fact that no changes occur in the process of activation of the left septal mass in right bundle branch block would indicate that no changes should take place in the ventricular complex in the first 0.01 second. However, the delay suffered by the wave of activation in passing from regions activated by the left branch to the first ramifications of the right branch theoretically should increase the magnitude and duration of the first septal vector, and, therefore, the Q wave would be expected to be more prominent. Experimentally, in cases like that of Fig. 13, we were able to observe this modification. In this experiment, special care was taken so that the position of the heart was the same in control conditions as it was after provoking block. Clinically, it is also possible to observe accentuation of the Q wave in leads oriented toward the lateral surface of the left ventricle as in the case corresponding to Fig. 14. This point should be watched carefully in clinical tracings, however, since vectorcardiographic tracings taken in different planes do not show, when normal and right bundle branch block curves are compared, any significant differences in their initial portions.

The diminution of the R wave, and the appearance of an S wave which increases in magnitude as the degree of block increases, corresponds to the manifestation of increasingly greater septal forces orientated from left to right that

predominate over the forces of the left ventricle. Our results suggest that during the inscription of the first portion of the S wave in Lead II, the obstruction to the passage of the wave of activation in the septum, already discussed at length, is still taking place. The later transeptal leads terminate synchronously with the notch of S in Lead II, so that only the final portion of this wave would correspond to the activation of the free wall of the right ventricle.

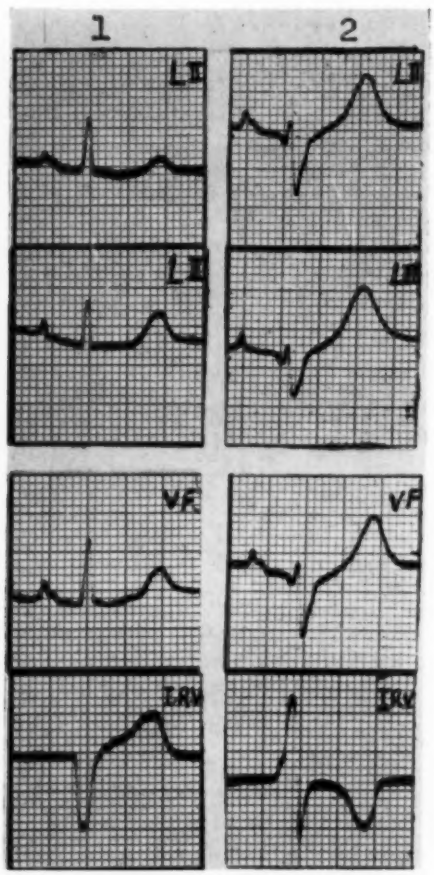


Fig. 13.—In Column *1* are shown control tracings corresponding to standard Leads II and III registered simultaneously, and Lead V_F registered simultaneously with an unipolar lead from the cavity of the right ventricle. Column *2*, after producing right bundle branch block. It should be mentioned that during the registration of all these leads, the position of the heart did not vary.

The statement that the activation of the free wall of the right ventricle in right bundle branch block corresponds principally to the final portion of QRS in Lead II is confirmed by the experiment illustrated in Fig. 15, in which it is seen that the inferior vertex of the intrinsic deflection of the unipolar epicardial lead from the right ventricle (in the tracing showing complete block; third tracing, Column 8) coincides exactly with the final portion of QRS in Lead II. Incidentally, it is interesting to note that the same tracing demonstrates quite clearly the very slight difference in the times of inscription of the endocardial and epi-

cardial tracings (separated only by the free wall). This is further confirmation of the previous observation that in bundle branch block the delay in conduction takes place in the septum and not in the free ventricular wall.

In this same figure, we would like to call attention to the initial slurring that is seen in the endocardial as well as the epicardial tracings with bundle branch block, and which is accentuated as the degree of block increases. The mechanism of this slurring is the basis for a special discussion in a study concerning the

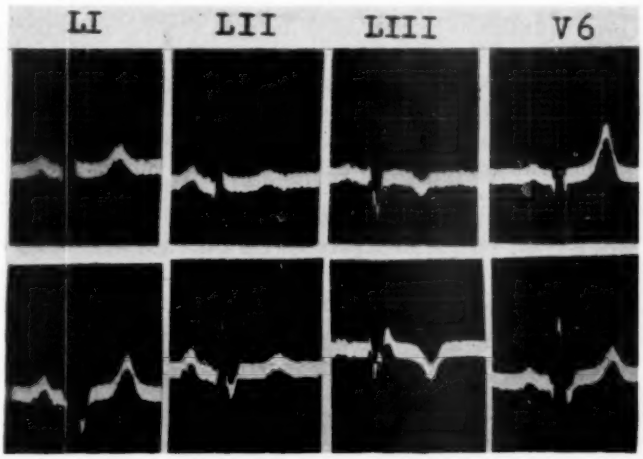


Fig. 14.—In the upper tracings a small negative deflection can be seen in standard Leads I, II, and precordial Lead V_6, oriented to the left ventricle. This negative deflection is accentuated when right bundle branch block appears (lower tracings).

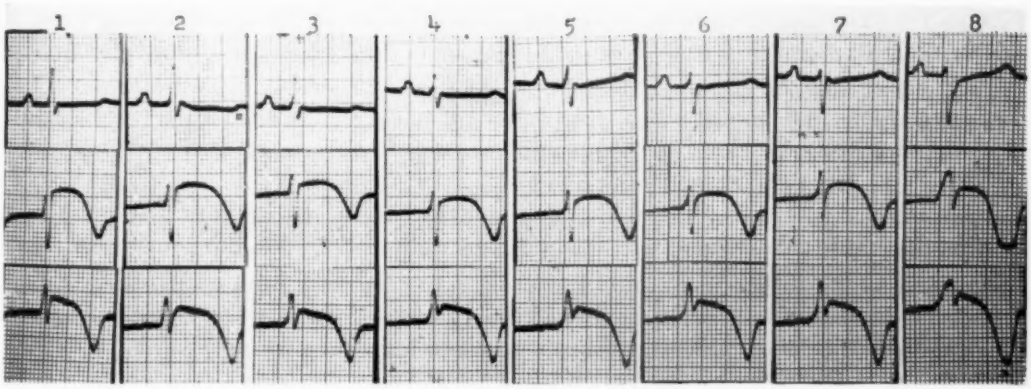


Fig. 15.—Endocardial and epicardial unipolar leads registered from the middle part of the free wall of the right ventricle, with both points situated on a line perpendicular to the ventricular surface. *1*, Control tracings: Lead II (upper tracing) registered simultaneously with the endocardial unipolar lead (middle tracing) and with the epicardial unipolar lead (lower tracing). *2* to *8*, The same leads as in *1* but with increasing grades of right bundle branch block.

activation of the free ventricular walls which we are now preparing. Nevertheless, we would like to advance the opinion that it is very probable that many clinical tracings with this type of initial slurring in the right precordial leads, such as those described by Zuckermann and associates[10] in certain congenital cardiopathies and by Cabrera and associates[11] in patent ductus arteriosus with pulmonary hypertension, correspond to incomplete right bundle branch block.

Recent studies[12] with direct epicardial leads from the right ventricle of the human heart during the surgical correction of certain congenital cardiopathies support this possibility.

In summary, the following conclusions can be formed regarding the mechanism of production of right bundle branch block:

1. In right bundle branch block, the speed and the sequence of the process of activation in the left ventricular septal mass are not modified. This is true in both complete and incomplete block.

2. In incomplete right bundle branch block, the right ventricular septal mass continues to be activated by the right bundle branch. Nevertheless, the process of activation is retarded depending on the degree of block. Consequently, bipolar transeptal leads are widened even with the slightest degrees of block, while the peripheral leads show only slight changes.

3. When the block reaches a certain degree, the wave of activation passes from the fibers activated by the left branch to those corresponding to the right branch. This passage (or jump) takes place in a very limited zone (about 2 mm.), very close to the right septal surface. It causes a delay in the process of activation of about 0.04 second, a delay that is responsible for the widening of the ventricular complex and, in great part, for the slurring of the S wave in the peripheral leads.

4. There are certain intermediate phases between the mechanisms of complete and incomplete block, in which the wave of activation passes from one ventricle to the other but in certain right ventricular portions of the septum continues to be activated by the right branch.

2. *Left Bundle Branch Block.*—Unlike what was observed in right bundle branch block, block of the left bundle branch produces modifications in the propagation of the wave of activation in the left septal mass.

With minor degrees of block, the direction of activation continues to take place from left to right, as under control conditions (Fig. 6, lower tracing; Columns 1 to 5). The septal tracings, using close bipolar leads which are registered from the muscular mass of the septum, do not show any essential change in their morphology but do show a delay in the arrival of the wave of activation at all points in the left septal mass, this delay increasing with the degree of block. Greater degrees of block, although still showing the form of QRS in Lead II which are usually interpreted clinically as incomplete block, demonstrate a reversal of direction of the wave of activation in the entire septal mass, the direction under these conditions being from right to left (Column 6, Fig. 6).

When the direction of the process of activation has been reversed by advanced degrees of left block, the close bipolar leads taken with the two electrodes located in the left septal mass show increased widening of the complex as the degree of block increases (Columns 7 to 9, Fig. 6).

The differences between the times of activation of those regions of the left septal surface and of those of the left septum proximal to the right septal surface are about 0.02 second with the maximum degree of block obtained. The speed of propagation in all the left septal mass, which under control conditions is from 1,000 to 1,200 mm. per second, diminishes. The values found with the greatest degrees of block are close to 350 mm. per second. This figure is similar to that given by Lewis[4,5] for the velocity of conduction in ventricular muscle. This would suggest that this type of conduction contrary to the usual direction takes

place largely through the muscles rather than the Purkinje fibers which conduct the normally oriented impulses. In any event, it should be pointed out that this does not account for the most important delay in conduction observed in left bundle branch block.

With the greatest degrees of left bundle branch block, the arrival of the wave of activation at the left septal surface is delayed from 0.07 to 0.08 second, compared to the time of activation under control conditions.

Apart from this, however, with the greatest degrees of left bundle branch block which we obtained, activation of the left septal surface, even with considerable retardation, maintained the same sequence that existed under control conditions. These findings lead one to conclude that in left bundle branch block, as well as in right bundle branch block, the most significant delay occurs when the wave of activation passes from regions activated by the right branch to the first ramifications of the left branch. Once arriving at the left Purkinje network, however, it proceeds to activate the left septal surface in the normal sequence and direction, without any significant delay. This explains why the sequence of the times of arrival of the wave of activation at the left surface is approximately the same as that which exists under control conditions, even when the activation of the left septal surface is much delayed.

The QRS Complex in Lead II in Left Bundle Branch Block.—As was pointed out in the discussion relative to right bundle branch block, standard Lead II in the dogs records variations of potential essentially like those registered on the lateral surface of the left ventricle.

Under control conditions, the first portions of the left ventricle to be activated depend for their activation on the left branch of the bundle of His. For this reason it is to be expected that block of this bundle branch would modify the initial part of the ventricular complex. With slight degrees of block, such a modification may not be manifested in the peripheral leads. The only change which is seen at such times is a slight delay in the inscription of the vertex of R wave and a slight increase in its voltage, as compared to control tracings. It is very likely that these slight degrees of block occur frequently in clinical cases and are interpreted as left ventricular hypertrophy instead of incomplete left bundle branch block. We verified this in a study of the left intraventricular potential of the human heart.[13]

Even when the direction of activation is not reversed, if there is a significant delay in the septal mass, vectorial forces of an opposite direction are produced which come from right and left septal activations, and which are responsible for the initial slurring of the ascending limb of R in Lead II. Nevertheless, this slurring may be present with or without a Q wave in the ventricular complex of Lead II. According to the degree of block, the initial slurring of the upstroke of R in Lead II is more or less accentuated.

Maximal grades of left bundle branch block cause marked widening of QRS (up to 0.08 second) and the appearance of a plateau, the duration of which is approximately 0.04 second. This plateau is primarily a consequence of the delay undergone by the wave of activation on passing from those regions activated by the right branch to those which, before the block, were activated by the left

branch. Under these conditions, the inscription of the upstroke of R in the peripheral lead corresponds, in accordance with our septal tracing, to the activation of the right septal surface (Column 2, Fig. 9). Clinically, in leads oriented toward the left ventricle, similar changes are seen in the evolution of left bundle branch block. Fig. 16 shows the electrocardiogram of a patient with a clinical diagnosis of coronary atherosclerosis. In the first tracing, with the least degree of block, there is an initial slurring of the upstroke of R in those leads which reflect the potential of the lateral surface of the left ventricle (Leads I and V_5). In the second tracing, with a greater degree of block, the slurring is seen in all of the ascending limb of R. With the maximum degree of block (third tracing), the QRS complex shows a plateau with a notch similar to that observed in our experimental tracings.

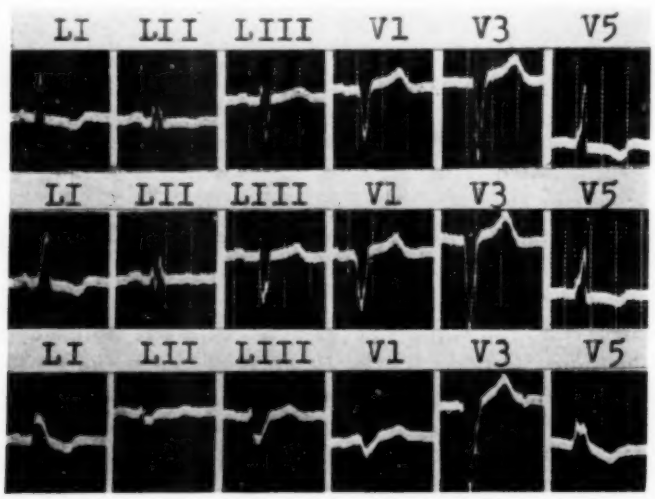


Fig. 16.—Electrocardiogram of a patient with coronary atherosclerosis. The upper row shows an incomplete left bundle branch block; the second row shows a greater degree of left bundle branch block, and the lower row shows a still greater degree of block. Note the changes in the morphology of the leads oriented toward the left ventricle (Leads I and V_6) in the evolution of the block.

In the majority of experiments, the inscription of the septal tracings are terminated almost at the end of the rapid ventricular complex in Lead II. This correlation again points to the necessity for insisting on the importance of the role of septal activation in producing a tracing of bundle branch block. This type of tracing has been attributed by some authors to delays in conduction that occur in the free ventricular walls (focal block).[14-18] We have observed no such delays in the free ventricular walls associated with this type of tracing.

In clinical electrocardiography, the appearance of a Q wave in peripheral leads which reflect the potential of the left ventricle, along with the presence of complete left bundle branch block, is suggestive of a septal infarction complicating the conduction disturbance.[19,20,21] It should be pointed out that changes in position of the heart make it possible for a Q wave to be present in Lead II in the presence of left bundle branch block without septal infarction and, at times, a

marked Q wave, such as is illustrated in Fig. 17. In this experiment, all the ventricular complexes show a morphology corresponding to complete left bundle branch block. In Column 1, the heart is in normal position, and in Columns 2 to 4 the apex points progressively toward the anterior chest wall, returning to the position of control in Column 5. With the apex directed anteriorly in this exaggerated manner, it is reasonable to assume that it records, fundamentally,

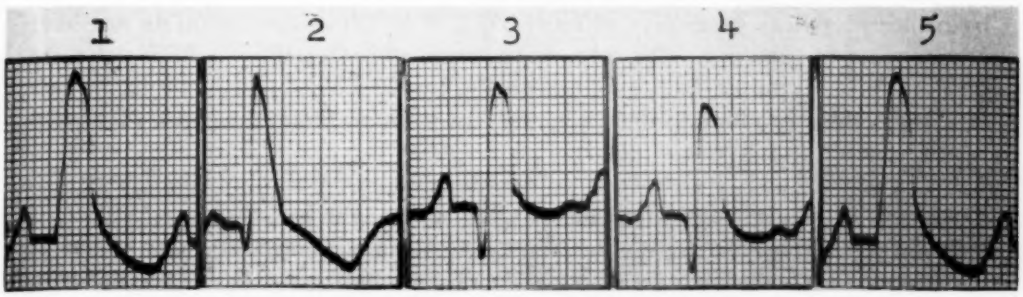


Fig. 17.—All the tracings are of standard Lead II with the maximum degree of left bundle branch block obtained. The heart was in normal position in Column *1*; in Columns *2* to *4* the apex was pointed progressively forward, returning to position of control in column *5*. Note the appearance of a negative initial deflection in Lead II when the apex is pointing forward.

Fig. 18.—Note the slurring or notching of the downstroke of R in the tracing corresponding to Lead II. This is in a dog's heart after the production of left bundle branch block.

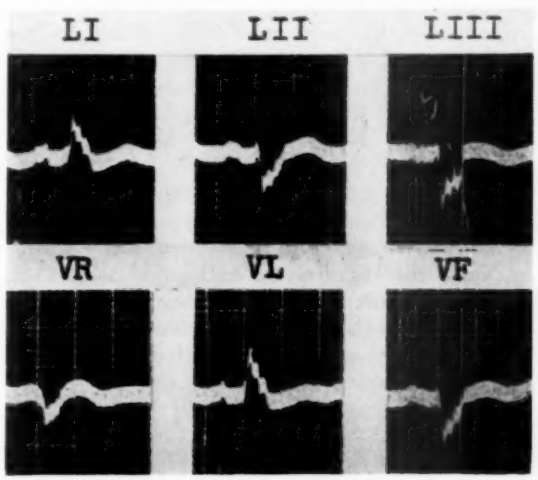


Fig. 19.—Left bundle branch block. Notching of the downstroke of R in the leads oriented toward the left ventricle (Leads I and V_L).

variations of potential of the left auricle. The same type of morphology is recorded directly from left auricle in the presence of left bundle branch block.

Another point that should be discussed is the presence of terminal slurrings of QRS in Lead II in left bundle branch block, which are registered generally in the descending limb of the R wave. Experimentally, we have produced these slurrings in the dog (Fig. 18) by section of the bundle branch, and they are similar to those observed in certain clinical tracings (Fig. 19). These changes have also been interpreted as suggestive of focal block.[16,18] Our experiments do not lend any support to this idea. We do not, however, eliminate the possibility of focal block. As a matter of fact, experimentally, by the use of drugs, we have been able to produce conduction delays in the free walls of the ventricles. (This will be the subject of a separate paper.)

The fact, already pointed out by various authors,[22,23] that left bundle branch block produced a greater duration of QRS than right bundle branch block is corroborated by our experiments. We have shown that in both types of blocks there is a delay in the passage of the wave of activation in a very limited zone of the septum, but in left bundle branch block there is, in addition, a moderate conduction delay in the left septal mass. Moreover, the sequence of activation of each of the ventricles favors the greater duration of QRS in left blocks.

In summary, the following conclusions relative to the mechanism of production of left bundle branch block can be made:

1. The speed and the sequence of the process of activation in the right septal mass undergoes no modification in complete or incomplete left bundle branch block.
2. In low degrees of left bundle branch blocks, the direction of activation in the left septal mass continues as under control conditions, from left to right. Nevertheless, the process of activation is retarded depending on the degree of block.
3. In incomplete blocks, activation of the right septal mass increases early in relation to activation of the left septal mass; this fact, in a given moment, can cause vectorial forces of opposite directions which are manifested by a notch in the bipolar transeptal leads and by an initial slurring of the R wave in the peripheral leads reflecting the potential of the left ventricle.
4. When the block reaches a certain degree, the wave of activation is transmitted from the fibers activated by the right branch to those corresponding to the left branch. This transmission is made in a very limited zone (2 mm.) proximal to the right septal surface, and causes a significant delay in the process of activation. This delay is the principal cause of the widening of the ventricular complex and the slurring of the R wave in the peripheral leads.
5. The zone in which this delay occurs seems to be the same for both right and left bundle branch block.
6. In complete blocks where "transmission" of the wave occurs, activation of the left septal mass takes place in the opposite direction (right to left), but with decreased speed (approximately 350 mm. per second) as compared to the control (1,200 mm. per second).
7. There are phases intermediate between the mechanisms pointed out for incomplete blocks and those for complete blocks, in which the wave of activation passes from one ventricle to the other, and invades some portions of the left septal mass. Other zones of the left septum which lie closest to the left septal surface are activated through the left bundle branch, although with some delay. Then, the activation of the septal mass, homolateral to the site of the block, is carried out by both branches.

Different Degrees of Bundle Branch Block.—Taking into account the physiopathologic mechanisms involved, three principal degrees of block can be delineated:

1. *Incomplete blocks.*—In this type, the stimulus continues to go by way of the injured branch but it is delayed in reaching the portions that depend on this branch for their activation.

2. *Complete blocks.*—In this type, the stimulus passes from the healthy branch to tissue that normally depends for its activation on the blocked branch.

3. *Intermediate blocks.*—In this type, the stimulus passes from the functioning branch to the tissue normally activated by the injured branch. However, the impulse continues to go by way of the injured branch with the result that the homolateral septal mass is activated by both branches.

SUMMARY

The propagation of the wave of activation in the interventricular septal mass of the dog's heart was studied under control conditions and with different degrees of bundle branch block.

Unipolar leads, differential leads with contiguous electrodes, and distant bipolar leads were recorded at different levels of the septum.

The following are the main findings:

1. Under control conditions the process of activation in the interventricular septum develops from left to right and below upward. The velocity of propagation in most of the septal mass, which is formed mainly by the left ventricular muscle, is very rapid, approximately 1,000 to 1,200 mm. per second; this suggests that the ramifications of the Purkinje penetrate deeply into the interventricular septum muscle.

2. Varying degrees of right bundle branch block do not modify the sense nor the sequence of the process of activation in the left ventricular mass so that the same velocity exists in the left ventricle as was found in control experiments.

3. Minor degrees of left bundle branch block cause a delay in the time of arrival of the wave of activation to all the left ventricular septal mass, but fail to modify the sense or the velocity of propagation within the same mass. When the degree of the block is of great magnitude, the sense of the activation is inverted in the whole left septal mass. This process is therefore carried out from right to left. Under these conditions, when the impulse propagates in a direction counterwise to the normal, the velocity of propagation within the left septal mass diminishes and in cases of complete block falls around 360 mm. per second.

4. In right as well in left bundle branch block there is a delay (approximately 0.03 to 0.04 second) which occurs in a relatively small portion of the septum (1.5 mm. to 2 mm.) very near the right septal surface. This delay occurs precisely when the impulse passes from the regions activated by the normally functioning branch to regions which were previously activated by the blocked branch. It is probable that the delay represents a latency in the propagation of the impulse in this zone. This suggests that the right and the left systems are functionally independent and thus eliminates the possible existence of communications between both branches. We believe that this is the first experimental evidence of the site where the delay takes place in bundle branch blocks.

5. The duration and importance of the septal phenomenon in the determination of ventricular curves is pointed out in normal conditions as well as in defects of intraventricular conduction.

6. The principal implications which have a bearing on clinical electrocardiography are discussed.

REFERENCES

1. Sodi-Pallares, D., Rodríguez, M. I., Chait, O., and Zuckermann, R.: The Activation of the Interventricular Septum, Am. Heart J. **41**:569, 1951.
2. Sodi-Pallares, D.: Nuevas Bases de la Electrocardiografía, México, 1951, Ed. Inst. Cardiol. México.
3. Sodi-Pallares, D., Thomsen, E., Barbato, E., Soberón, A. J., Fishleder, B. L., and Estandía, A.: Bloqueos Incompletos de Rama, Arch. inst. cardiol. México **18**:497, 1948.
4. Lewis, T., and Rothschild, M. A.: The Excitatory Process in the Dog's Heart. II. The Ventricles, Phil. Trans. Roy. Soc., Lond. **206**:181, 1915.
5. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, London, 1925, Shaw & Sons, Ltd.
6. Erlanger, J.: Observations on the Physiology of the Purkinje Tissue, Am. J. Physiol. **30**:395, 1912.
7. Lepeschkin, E.: Das Electrocardiogram, Dresden and Leipzig, 1947, Theodor Steinkopff.
8. Wilson, F. N., and Herrmann, G. R.: An Experimental Study of Incomplete Bundle Branch Block and of the Refractory Period of the Heart of the Dog, Heart **8**:229, 1921.
9. Fenichel, N.: An Analysis of the Complex of the Electrocardiogram, Am. Heart J. **7**:514, 1931-1932.
10. Zuckermann, R., Cisneros, F., and Novelo, S.: El Electrocardiograma en Algunas Cardiopatías Congénitas, Arch. inst. cardiol. México **21**:51, 1951.
11. Cabrera, E., Borges, S., and Novelo, S.: Estudio Electrocardiográfico de la Persistencia del Conducto Arterioso, Arch. inst. cardiol. México **20**:426, 1950.
12. Carouso, G., Chevalier, H., Latscha, J., and Lenegre, J.: Epicardial Electrocardiograms Recorded in the Course of Seven Cases of Heart Surgery, Circulation **5**:48, 1952.
13. Sodi-Pallares, D., Estandía, A., Soberón, A. J., and Rodríguez, M. I.: The Left Intraventricular Potential of the Human Heart. II. Criteria for Diagnosis of Incomplete Bundle Branch Block, Am. Heart J. **40**:555, 1950.
14. Vastasaeger, M. M.: Les troubles de la conduction intraventriculaire chez l'homme, Acta cardiol. **1**:1, 1946.
15. Segers, M.: Le déterminisme des courbes de prépondérance, Acta cardiol. **5**:288, 1950.
16. Segers, M., Vastasaeger, M., and Denolin, H.: Les différents aspects des troubles de la conduction intraventriculaire, Acta cardiol. **2**:166, 1947.
17. Segers, M.: Les voies de conduction intraventriculaire, Arch. internat. de physiol. **57**:220, 1949.
18. Segers, M.: The Different Types of Intraventricular Block, Am. Heart J. **37**:92, 1949.
19. Wilson, F. N.: The Electrocardiogram in Diseases of the Coronary Arteries, *in* Levy, R. L.: Diseases of the Coronary Arteries and Cardiac Pain, New York, 1936, The Macmillan Company.
20. Sodeman, W. A., Johnston, F. D., and Wilson, F. N.: The Q_1 Deflection of the Electrocardiogram in Bundle Branch Block and Axis Deviation, Am. Heart J. **28**:271, 1944.
21. Sodi-Pallares, D., and Rodríguez, M. I.: Morphology of the Unipolar Leads Recorded at the Septal Surfaces. Its Application to the Diagnosis of Left Bundle Branch Block Complicated by Myocardial Infarction, Am. Heart J. **43**:27, 1952.
22. Rothberger, C. J., and Winterberg, H.: Experimentelle Beitraege zur Kenntnis der Reizleitungs-Stoerungen in den Kammern des Saeugetierherzens, Z. Exper. **5**:264, 1917.
23. Alfredson, B. V., and Sykes, J. F.: Studies on Bovin Electrocardiogram. II. Bundle Branch Block, Proc. Soc. Exper. Biol. & Med. **43**:580, 1940.
24. Burchell, H. B., Pruitt, R. D., and Essex, H. E.: Excitation of the Isolated Ventricular Septum of the Heart, Proc. Soc. Exper. Biol. & Med. **77**:117, 1951.

ON SOME ASPECTS OF UNIPOLAR ELECTROCARDIOGRAPHY IN THE PRESENCE OF PULMONARY PATHOLOGY

THEODORE T. FOX, M.D., HERBERT BERGER, M.D., AND CHARLES E. MEIDT, M.D.

STATEN ISLAND, N. Y.

IN THE presence of pulmonary disease the electrocardiographic tracing is frequently abnormal. The abnormality does not present a specific pattern, and differentiation, therefore, between myocardial damage and cardiac displacement secondary to lung pathology is at times a difficult task. Some of our experiences with the abnormal electrocardiogram at Sea View Hospital, an institution for the care of tuberculosis, have been reported in previous publications.[1,2,3] This communication will deal with the contribution made by the unipolar leads toward the graphic differentiation between intra- and extracardiac disease.

MATERIAL AND RESULTS

One hundred unselected tracings, presenting some abnormality in any of the auricular or ventricular complexes, were chosen for analysis. The clinical records of the patients with these abnormal electrocardiograms were reviewed, and some of the doubtful cases were re-examined physically and fluoroscopically, so that a fair degree of correlation was achieved between the clinical impression of the patient and his electrocardiographic tracing. Tracings presenting auricular fibrillation and other arrhythmias, as well as those showing bundle branch block, were excluded. The entire group in this study had pulmonary tuberculosis, unilateral or bilateral. Some of the patients had moderately advanced disease while others presented considerably advanced pulmonary pathology. A few of the patients had an artificial pneumothorax at the time the electrocardiogram was secured. With an occasional exception (see below), none presented evidences of intrinsic heart disease. The age distribution was as follows: second decade, seven cases; third decade, twenty cases; fourth decade, nineteen cases; fifth decade, eighteen cases; sixth decade, eighteen cases; over 60 years, eighteen cases.

The abnormalities noted in the standard leads were as follows (Table I): Abnormal P wave, forty-three cases (P wave was considered abnormal if it was taller than 3 mm., notched, spiked, isoelectric, or inverted in Lead I or II.) Deviation in the RS-T segment, twenty-one cases. In twenty cases the RS-T

From the Department of Cardiology, Sea View Hospital, Staten Island, N. Y.
Received for publication July 7, 1952.

TABLE I. INCIDENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES IN VARIOUS LEADS

	ABNORMAL P WAVES	RS-T		T INVERSION	OTHER T-WAVE ABNORMALITIES	VARIABLE T WAVE IN SAME LEAD	FLUCTUATING QRS VOLTAGE	s1-2-3 PATTERN	DEEP Q WAVES	R/S IN PRECORDIAL LEADS		P▼ RT▼
		DEPRESSION	ELEVATION							CLOCKWISE	COUNTERCLOCKWISE	
Standard leads	43	20	1	39	(dome) 6	4	3	1	3			
Wilson leads	14	7	6	21	15				2	12	1	
aV_R		1	3		3							
aV_F	13	12	1	18		5			2			
aV_L	24	3		18					1			22

segment was depressed and in one case it was elevated (RT_3). (Fig. 1.) Abnormal T waves, forty-five cases. In thirty-nine cases the T wave was inverted and in six cases it was dome-shaped. Changes in T_3 were not included. Varying T waves in same lead, four cases. Fluctuating voltage of the QSR complex, three cases. S1-2-3, one case. Deep Q_2 and Q_3, two cases. Deep Q_1 and Q_3, one case. (Fig. 2.)

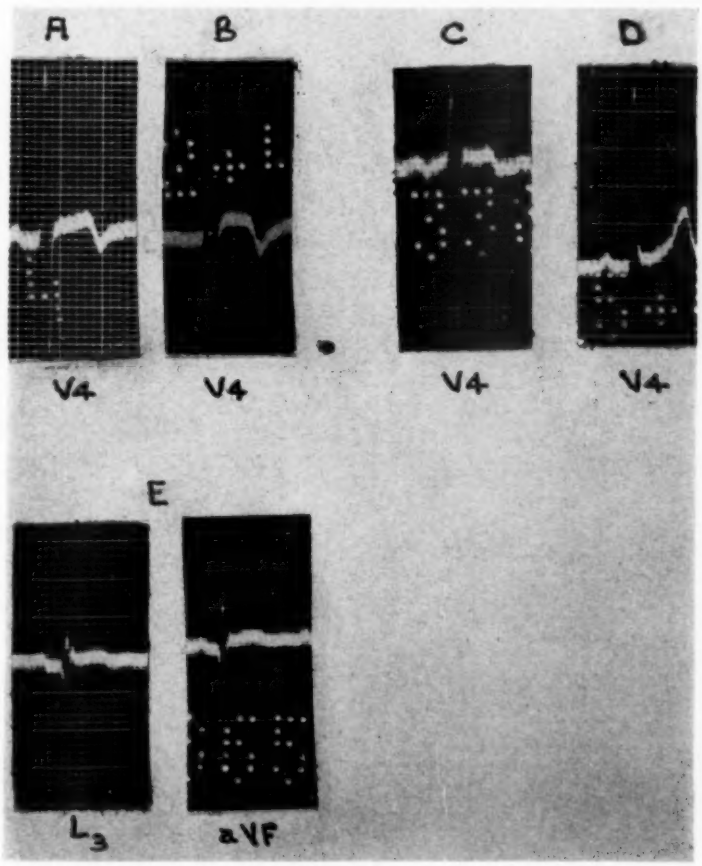


Fig. 1

The abnormalities noted in the Wilson unipolar precordial leads were as follows (Table I): Abnormal R/S ratio indicative of clockwise rotation, twelve cases; abnormal R/S ratio indicative of counterclockwise rotation, one case; abnormal P waves in fourteen cases; in three cases only the P wave in V_1 was abnormal (not inverted). In one case the P wave was abnormal all across the precordium. Notching of the P wave was observed only once. R-T depression was observed in seven cases. In three cases this finding was seen only in V_5 and V_6. RS-T elevation was seen in six cases. One case presented elevation of R-T in V_1; one in V_1 and V_2, and one in V_2 and V_3. Two cases had elevation in V_5 and V_6. One case showed elevation all across the precordium. The T wave was upright in V_1 in nine cases, variable in one or more V leads in six cases, inverted all across the precordium in eight cases, in some but not in all V leads,

in twelve cases. In one case V_2 and V_3 presented an upright T, V_4 a deeply inverted T wave, and V_5 and V_6 a low amplitude T wave. Low voltage QRS complexes were seen in one case. In one case the R was labile in voltage. Significant (?) Q waves were seen in two cases.

The abnormalities noted in aV_R were as follows (Table I): Depression of RS-T segment, one case; elevation of RS-T segment, three cases; upright T wave, one case; variable T wave, two cases; variable QRS voltage, one case; and low voltage QRS, one case. There were no abnormalities in the structure of the P wave.

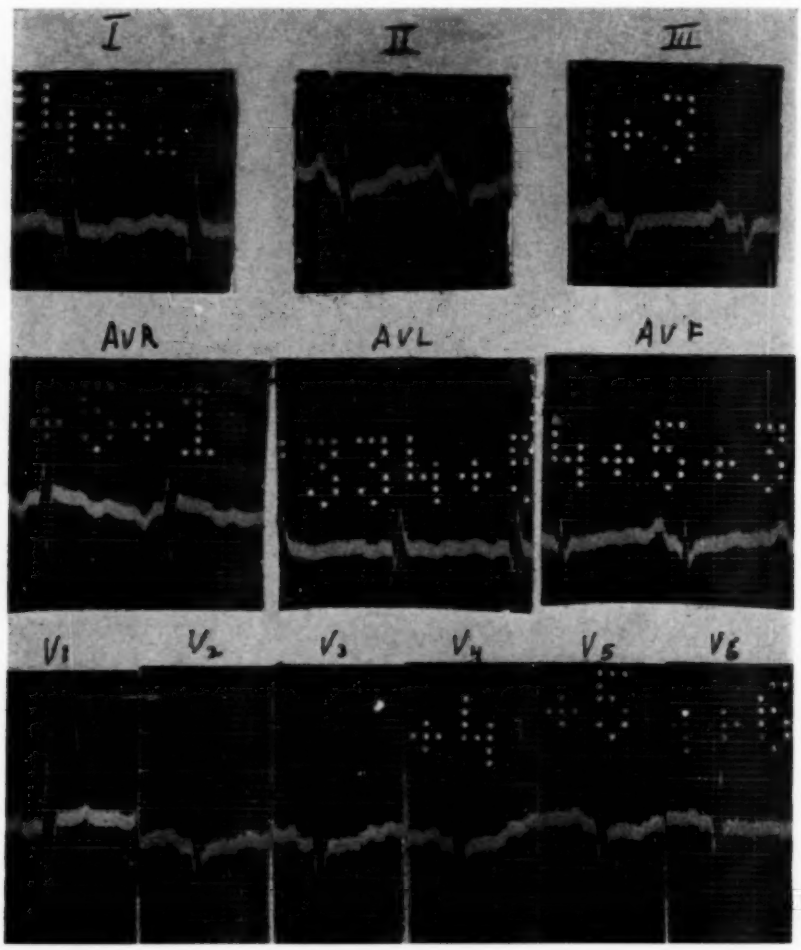


Fig. 2

The abnormalities in aV_L were as follows: The P wave was abnormal in twenty-four cases. Some P waves were isoelectric, some diphasic, and some inverted. None of the abnormal P waves were tall or spiking. A QR complex was noted twice, QS once. A deep Q wave was seen once (Q, 3 mm., R, 2 mm., P and T inverted in a boy 20 years old with a left pneumothorax). The RS-T segment was depressed three times. In one case the depressed R-T segment

was associated with an inverted P wave and a fluctuating amplitude of the T wave. This patient had hypertensive heart disease, and the rest of the electrocardiographic tracing was that seen in left ventricular hypertrophy. Elevation of the RS-T segment was not observed. The T wave was inverted in eighteen cases. In two of the eighteen cases the T wave was unstable.

A pattern consisting of an inverted P wave, an R wave, and an inverted T wave was seen twenty-two times. In this group left-axis deviation was noted thirteen times, no axis deviation eight times, and the pattern of S1-2-3 once. The transitional zone in the V leads was anywhere between the second and fifth precordial positions. The amplitude of the R wave was 10 or more mm. in six cases; in fourteen cases the amplitude of the R wave was between 5 and 10 mm.; in two cases it was less than 5 mm. aV_R was abnormal in every case. In one case a QS and QR were seen to alternate in the available strip. aV_F presented an RS four times, Rs twice, and R, eight times; rS was seen three times. The rest of the cases presented a qR or a qRs pattern. The T wave in aV_F was inverted five times, of low amplitude five times, and upright twelve times. Apparently the above-described PRT configuration in aV_L was independent of changes in aV_R or aV_F. The clinical or roentgenologic picture in this special PRT group presented no constant uniform abnormality.

The abnormalities in aV_F were as follows: The P waves were abnormal thirteen times; none were inverted. They were mostly tall or notched. Deep Q waves were seen twice. In one case the width of the Q wave was 0.04 second. The patient gave no history and presented no evidence of myocardial damage. In the second case the duration of the Q wave width was 0.06 second. The patient, age 63 years, had hypertensive heart disease and peripheral arteriosclerosis obliterans. The electrocardiogram showed a deep Q_2 and Q_3 in addition to a depressed RT_1, and R-T depression in aV_L. It was assumed that the patient had a silent posterior infarct. Low-voltage QRS complex was seen in one case (same as the one in aV_R). RS-T was depressed twelve times, elevated once (Fig. 1). The T wave was inverted eighteen times and variable in five cases.

Of the one hundred abnormal tracings, only four were recognized as indicative of myocardial damage; and the existence of such disease was confirmed clinically. This figure is in line with the incidence of heart disease at Sea View Hospital. The tracings were interpreted as denoting disease on the basis of the following findings:

CASE 1.—M.Z., age 63 years, high voltage, RT_1 depressed, Q_2, 7 mm., Q_3, 10 mm.—0.09 wide. RT in V_5 depressed, S-T in aV_L depressed, Q in aV_F 8 mm., and QT prolonged (hypertension, arteriosclerosis obliterans, and silent coronary thrombosis). Evidences of mediastinal shift were: variable RS-T segments in V_5 and variable P waves in aV_L.

CASE 2.—I.S., age 61 years, left axis deviation, high voltage, R-T depression in V_5, R-T depression in aV_L, QT prolonged (hypertension). Evidence of displacement, none.

CASE 3.—J.K., age 73 years, left axis deviation, high voltage, first stage atrioventricular block, Q_{2-3} deep and wide, Q_1 small, Q waves across precordium, T inversion across precordium, T in aV_L inverted, Q in aV_F deep. Patient had a history of coronary insult. Evidence of displacement: variable P waves in aV_L, aV_F, and precordial leads, notched P wave in Lead I.

CASE 4.—W.P., age 43 years. Classical evidence of cor pulmonale including a late R′ in V_1. Evidence of mediastinal shift, fluctuating amplitude of R′ from 2 to 9 mm.

DISCUSSION

While definite statistical conclusions can not be drawn from this study, one gets the impression that in the material presented no evidence of myocardial damage was present in the unipolar leads that was not already discernible in the standard leads. The contributions made by the unipolar leads in this study were: (1) They helped to explain abnormalities in the standard leads, and (2) they added evidence of mediastinal shift and rotation in those instances where the standard leads appeared normal to first examination. The interpretation of displacement was confirmed by the Wilson and unipolar extremity leads in twenty-one cases, was assisted in nineteen cases, and dependent entirely upon the Wilson and unipolar extremity leads in eight cases. In forty-one cases the Wilson and unipolar extremity leads did not assist in making a diagnosis of mediastinal shift. This study further emphasizes the part played by the P wave in the diagnosis of displacement of the heart,[1] the unreliability of the T wave as an indicator of myocardial damage, and the caution with which RS-T changes and even Q waves should be viewed when considering muscle damage. While such abnormalities occur in apparently normal chests,[4,5] there seems to be no question that pulmonary pathology greatly increases their frequency. Therefore, great caution should be exercised in the interpretation of electrocardiograms under such circumstances.

A note about the RS-T elevations: According to Myers and associates,[4] "An elevation of the RS-T junction may be considered within normal limits if the displacement does not exceed 2.0 mm., and provided that the RS-T segment immediately begins to rise above the junction in an arc with upward concavity to end in a tall upright T wave." Such is the case in *D*, Fig. 1. In cases of pulmonary pathology, however, the T wave may be diphasic or inverted (Fig. 1,*A*,*B*,*C*) in some or all V leads, in the presence of an elevated RS-T segment. A more spectacular illustration of this phenomenon was given in a previous publication.[2] The R-T elevation was 4 mm. above the isoelectric line.

The pathogenesis of these electrocardiographic changes is not the subject of this communication. Suffice it to say that we believe that anatomic variations and anatomic instability of the mediastinum seem to be a major factor in their genesis. In many cases it is possible to produce a T wave as well as RS-T changes by merely altering the patient's position. We find this technique valuable diagnostically. It is our impression that positional changes are more easily obtained in the younger age group. This observation presents a point of contact between our group and that of normal young people with abnormal electrocardiograms reported by others.[6-9] Again we observed this phenomenon more frequently than in similar age groups without chest pathology. Apparently lung pathology alters the mediastinum of these people, disturbing the physiologic as well as the anatomic equilibrium, producing abnormalities, single or multiple, in the components of the electrocardiogram, stationary or fluctuating. The variations, when present, are not necessarily phasic.

Regarding the contribution made by the unipolar leads in this limited study, the incidence of the PRT configuration in aV_L described above deserves emphasis. It was observed twenty-two times. It was totally independent of the configuration of aV_R which frequently was either of the QS or rS type, differing in

this respect from the experience of Goldberger.[10] None of the twenty-two cases with this electrocardiographic phenomenon had any clinical evidence of cardiovascular disease.

SUMMARY AND CONCLUSION

In a group of one hundred abnormal tracings of patients with pulmonary tuberculosis, four electrocardiograms were interpreted as being due to myocardial damage, and ninety-six were apparently due to mediastinal shift and rotation.

The abnormalities in the various leads were noted. It appeared that multiple unipolar chest and augmented unipolar extremity leads did not aid materially in the differentiation of damage from displacement. They served, instead, to help in the explanation of the abnormalities in the standard leads. In the course of this study some findings of note were recorded: Deviation of the RS-T segment is not necessarily associated with myocardial damage and a pattern consisting of an inverted P wave and R wave and inverted T wave in aV_L frequently occurs in mediastinal displacement.

The RS-T deviations as well as the T changes in the precordial leads in the electrocardiogram of patients with pulmonary pathology demand particular caution in their interpretation.

REFERENCES

1. Fox, T. T., and Kremer, H. S.: The Heart in Pulmonary Tuberculosis, Am. Rev. Tuberc. **47**:135, 1943.
2. Fox, T. T.: The Electrocardiogram in Chest Diseases, Tuberculology **11**:11, 1949.
3. Fox, T. T., and Fishman, L.: The Electrocardiogram in Pneumothorax, Quart. Bull. Sea View Hosp. **9**:305-311 1947.
4. Myers, G. B., Klein, H. A., Stofer, B. E., and Hiratzka, T.: Normal Variations in Multiple Precordial Leads, Am. Heart J. **34**:785, 1947.
5. Graybiel, A., McFarland, R. A., Gates, D. C., and Webster, F. A.: Analysis of the Electrocardiograms Obtained From 1,000 Healthy Young Aviators, Am. Heart J. **27**:524, 1944.
6. Graybiel, A., and White, P. D.: Inversion of the T-wave in Lead I or II of the Electrocardiogram in Young Individuals With Neurocirculatory Asthenia, With Thyrotoxicosis, in Relation to Certain Infections, and Paroxysmal Ventricular Tachycardia, Am. Heart J. **10**:345, 1935.
7. Wendkos, M. H., and Logue, R. B.: Unstable T-waves in Leads II and III in Persons With Neurocirculatory Asthenia, Am. Heart J. **31**:711, 1946.
8. Littman, D.: Abnormal Electrocardiograms in the Absence of Demonstrable Heart Disease, Am. J. Med. **5**:337, 1948.
9. Marvel, R. J., and Failey, R. B.: Unusual Precordial Lead Patterns in the Exercise Tolerance Test, J. Lab. & Clin. Med. **38**:926, 1951.
10. Goldberger, E.: Unipolar Lead Electrocardiography, Philadelphia, 1949, Lea & Febiger, p. 109.

ELECTROCARDIOGRAPHIC AND SERUM POTASSIUM CHANGES IN FATAL HYPERTHERMIA

LEON I. GOLDBERG, PH.D.,* HUMPHREY K. EZELL, M.S., AND ROBERT P. WALTON, PH.D., M.D.

CHARLESTON, S. C.

ALTHOUGH electrocardiographic records obtained during various types of febrile states have often been described, there have been very few studies concerned with the electrocardiographic changes occurring during fatal hyperthermia. In a recent investigation of the cardiovascular effects of hyperthermia produced by dinitrophenol, large doses of Dicumarol, and by externally applied heat, marked electrocardiographic changes were consistently observed.[1] In these preceding experiments, anestheti ed dogs in an advanced state of hyperthermia were observed through progressive changes to fatal termination. The characteristic electrocardiographic pattern associated with the hyperthermia consisted of extreme sinus tachycardia, heightened T waves, S-T depression, and, terminally, disappearance of the P wave, widening of the QRS complex, and ventricular fibrillation or cardiac arrest. As most of these changes resemble the effects produced by high serum potassium levels, the present study was primarily undertaken in order that serum potassium levels could be determined in similar hyperthermia experiments and correlated with the electrocardiographic changes. Additionally, the course of study was designed so that other blood chemical and cardiovascular changes produced by hyperthermia could be observed and their influence on the electrocardiogram similarly evaluated.

REVIEW OF THE LITERATURE

Prior to the recent report from these laboratories, electrocardiographic effects with fatal calorigenic doses of Dicumarol had not been published, although Carlson and Seager[2] had reported the occurrence of ventricular fibrillation in small animals dying from overdosages of Dicumarol. Lequime and Denolin[3] observed marked T-wave changes, auricular fibrillation, ventricular premature contractions, and ventricular fibrillation in dogs made hyperthermic with large doses of

From the Departments of Pharmacology and of Chemistry, Medical College of South Carolina, Charleston, S. C.

Preliminary abstract in Federation Proc. **11**:348, 1952.

This investigation was supported by research grants from the National Heart Institute, United States Public Health Service.

The supplies of Dicumarol and of Tromexan were obtained through the courtesy, respectively, of Dr. A. E. Osterberg, Abbott Laboratories, North Chicago, Ill., and Dr. A. Hemming, Geigy Company, Inc., Pharmaceutical Division, New York, N. Y.

Received for publication June 25, 1952.

*Fellow of the American Foundation for Pharmaceutical Education, 1949-1952.

dinitrophenol. Brewer[4] reported that hyperthermic doses of dinitrophenol administered to cats and dogs produced high serum potassium levels which appeared to be related to increments in body temperature rather than to absolute levels of temperature.

Cheer[5] took serial electrocardiograms of dogs fatally heated by radiation from electric light bulbs in specially designed cabinets. He observed that the P-R interval became shortened, the QRS decreased in amplitude and often became notched, and the inverted T wave became upright. Ultimately, at the very end, atrioventricular block and various types of ventricular arrhythmias developed. Giovanni[6] observed sinus tachycardia, nodal rhythms, ventricular premature contractions, paroxysmal tachycardia, and auricular and ventricular fibrillation in rabbits subjected to the temperatures of a heat cabinet. Roos, Weisiger, and Moritz[7] found greatly elevated plasma potassium levels with accompanying hyperpotassemic electrocardiographic changes in pigs killed by sudden immersion in water heated to 75° C. The high potassium levels were explained mainly on the basis of the severe hemolysis which took place. With dogs, similarly scalded, increased potassium levels were not observed, this being attributed to the fact that the dog, unlike the pig, does not have high erythrocyte potassium values.

The effects of hyperpotassemia on the electrocardiogram have recently been comprehensively reviewed by Levine and associates[8] and by Merrill.[9]

METHODS

Twenty-nine mongrel dogs were used in these experiments. The animals were anesthetized by intravenous administration of either Dial with Urethane (50 mg./kg.) or by the combination of pentobarbital sodium (15 mg./kg.) and barbital sodium (225 mg./kg.). As in the previous study, all animals were subjected to bilateral cervical vagotomy and were administered oxygen by interrupted pressure through a tracheal cannula; active respiratory movements were permitted through the side arm of a T tube.

Hyperthermia was produced in ten of the dogs by use of General Electric household heating pads and radiation from infrared bulbs. The animals were wrapped in burlap bags and the heat pads were placed over the abdomen and under the back. The infrared bulbs were placed about 10 cm. above the abdomen and were used only when sufficient heat production could not be obtained by use of the heat pads alone. Heat intensity was controlled by a variable transformer (Variac).

Eleven dogs were made hyperthermic by intravenous infusion of Dicumarol in doses of 30 or 50 mg./kg. administered over a thirty-minute period. Three dogs were administered dinitrophenol, similarly, in 10 mg./kg. doses.

Frequent electrocardiograms were obtained in every experiment by a direct-writing Cardiotron manufactured by the Electro-Physical Laboratory. A precordial lead, usually V_4, was obtained in every experiment; limb Lead II was also successively recorded in most experiments. Hypodermic needle electrodes were used throughout.

TABLE I

EXPERIMENT (NO.)	METHOD OF HYPERTHERMIA (Mg./Kg.)	CONTROL		ELEVATION OF T WAVE		LOSS OF P WAVE		INTERVAL BETWEEN PRECEDING K DETERMINATION AND LOSS OF P WAVE (MIN.)	POST MORTEM SERUM K (Mg. %)	TIME FOR DEATH (MIN.)	TEMP. AT DEATH (°C)
		SERUM K (Mg. %)	TEMP. (°C)	SERUM K (Mg. %)	TEMP. (°C)	SERUM K (Mg. %)	TEMP. (°C)				
1	Dicumarol 30	20	36.5	—	38.2	41	44.5	45	46	185	44.5
3	Dicumarol 50	22	36.4	—	41.8	42	42.8	0	42	197	43.0
4	Dicumarol 50	22	38.8	—	40.8	31	44.7	7	39	66	46.0
5	Dicumarol 50	18	38.9	22	40.5	35	45.6	0	47	66	45.6
6*	Dicumarol 50	20	38.6	26	40.2	37	44.0	0	37	47	44.5
7	Dicumarol 30	18	37.8	29	39.5	39	44.3	0	40	78	44.5
8	Dicumarol 30	19	37.4	—	42.7	34	44.0	5	38	92	44.0
9	Dicumarol 30	16	38.1	No T-wave elevation		33	45.5	0	33	65	45.8
10*†	Dicumarol 50	22	37.7	No T-wave elevation		32	44.7	0	34	48	45.0
11*†	Dicumarol 30	17	36.4	21	38.1	34	44.0	1	34	79	44.0
12*†	Dicumarol 30	19	37.2	26	41.4	30	46.0	65	40	151	46.0
18*†	DNP‡ 10	24	38.2	27	40.1	34	45.0	2	46	84	45.0

19*†	DNP	10	23	38.2	26	39.4	32	43.1	22	63	59	43.1
23*†	DNP	10	20	37.3	—	38.6	47	45.4	0	61	52	45.7 (Fig. 1)
2	Heat		17	39.3	20	39.6	27	43.0	9	61	65	43.0
13†	Heat		20	39.4	23	41.2	38	45.3	10	42	75	45.3
14†	Heat		23	36.3	27	40.3	35	44.0	23	49	142	45.1
15*†	Heat		18	35.1	—	38.0	31	42.4	25	76	103	42.4
16*†	Heat		16	38.5	—	41.0	30	44.6	26	60	157	44.6 (Fig. 3)
17*†	Heat		16	37.4	25	41.2	25	41.2	0	70	168	45.0
20†	Heat		19	37.6	No T-wave elevation		28	45.0	2	36	273	45.0
21	Heat		17	37.3	22	40.5	38	44.8	0	40	226	44.9
22†	Heat		21	35.6	23	42.4	34	45.0	6	34	97	45.0
24*†	Heat		20	38.0	26	41.0	36	43.5	0	58	113	43.5 (Fig. 2)

*Experiment included contractile force recordings.
†Experiment included blood pressure recordings.
‡DNP, Dinitrophenol.

Potassium and sodium determinations were obtained in most cases from arterial blood drawn from a femoral or carotid artery. In a few experiments, femoral venous blood was used. Immediately after death, in each experiment, the thorax was opened and blood samples were drawn from the right ventricle by cardiac puncture with a 15-gauge needle. The latter procedure was completed within three to ten minutes of cessation of the heart beat.

Serum and whole blood potassium and sodium samples were analyzed by a Perkin-Elmer Flame Photometer. Serum and whole blood hemoglobin determinations were made by use of a Lumetron Colorimeter. Venous and arterial oxygen contents were determined either manometrically by the Van Slyke-Neill method or colorimetrically by the NAC-11 "N" Cuvette and Beckman Spectrophotometer. Serum calcium levels were determined by oxalate precipitation and potassium permanganate titration. Volume of packed cells was determined by the use of the Wintrobe hematocrit spun for thirty minutes at 15,000 revolutions per minute.

Eleven animals were prepared for contractile force measurement by the attachment of a strain gauge arch to the right ventricle as has been previously described.[10] Arterial blood pressure was obtained in fourteen experiments from a carotid artery by a Statham Transducer and Brush Strain Analyzer (BL-310) and oscillograph (BL-202). In two experiments with Dicumarol not listed in Table I, ligatures were placed around the thoracic aorta at the level of the seventh intercostal space so that aortic compression could be carried out during the experiment. Temperatures in all experiments were measured by means of a mercury bulb thermometer inserted into the rectosigmoid about 20 cm. beyond the anal orifice. Rectosigmoid temperatures, under these conditions, have been found to correspond closely to thermocouple recordings of vena caval and myocardial temperatures.[1]

The pH of unclotted arterial blood was obtained in one of the experiments with Dicumarol and one with external heat application by a Beckman pH meter.

Three additional experiments were conducted with the Dicumarol derivative, Tromexan, (ethyl biscoumacetate). The drug was infused intravenously in a dose of 65 mg./kg. in one experiment and 100 mg./kg. in the others. These experiments are not included in the table and results are discussed separately. The Tromexan solution was prepared by addition of sodium hydroxide until a pH of about 9 was reached and was administered in 1 per cent strength.

RESULTS

Serum potassium levels rose in every experiment. The average of the control levels was 19.5 mg. per cent S.D. ±2.3 (5.0 meq./L.). Fig. 1 illustrates typical precordial (V_4) electrocardiograms obtained in an experiment with dinitrophenol correlated with serum potassium and rectosigmoid temperature determinations. Fig. 2 illustrates the similar changes produced by external heat application.

The first electrocardiographic pattern change in the majority of experiments was heightening or peaking of the T wave. The T wave usually became more prominent in the precordial lead than in the limb lead, as has been reported by Finch, Sawyer, and Flynn.[11] The temperature and serum potassium levels at

which the T-wave changes first took place are shown in Table I. Only those potassium determinations are included which were obtained at closely the same time as the first T-wave change. The average serum potassium level at which heightening of the T wave took place with the calorigenic drugs was 25.3 mg. per cent S.D. ±2.8; the average temperature was 40.1° C. ±1.3. With external heat, the average serum potassium level was 23.7 mg. per cent±2.4, the average temperature 40.6° C. ±1.2. In only two experiments with Dicumarol and one with external heat was there no elevation of the T wave, despite rising potassium levels. In Experiment 9, the T wave was slightly upright initially, but became inverted and remained so throughout the experiment. In Experiment 10, there was a high peaked T wave in the control which did not change in height. In Experiment 20, the T wave was initially slightly inverted and became progressively more deeply inverted as the serum potassium levels rose.

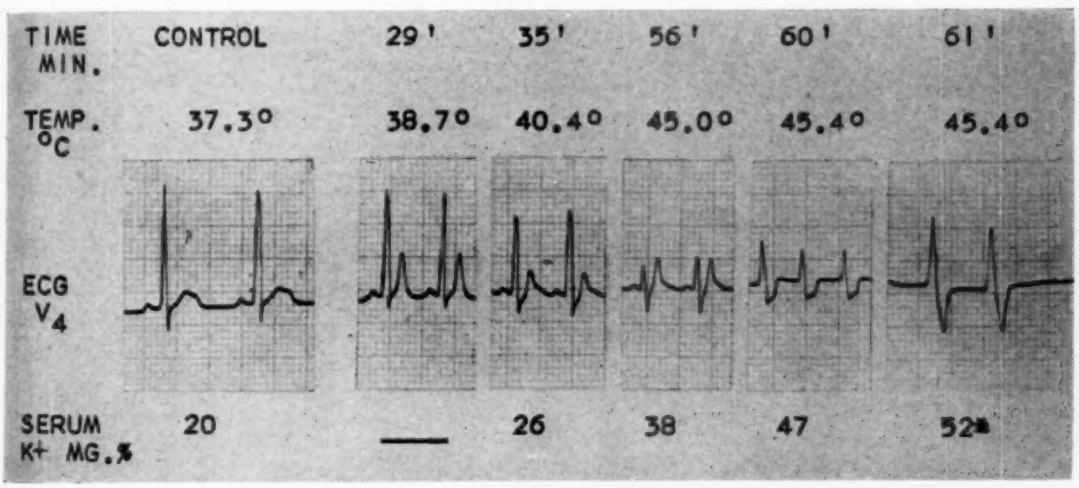


Fig. 1.—Selected electrocardiographic tracings (V_4) of the progressive effects in an anesthetized dog given 10 mg./kg. of dinitrophenol by intravenous infusion during a period of thirty minutes. Temperatures taken from rectosigmoid area. The final serum potassium level was obtained from the right ventricle immediately after death.

S-T depression occurred in most experiments. In the majority of cases, this change followed the onset of T-wave changes. Deep S-T depression with a biphasic T wave was commonly seen in the later stages; this pattern was more typical in limb Lead II and in some instances was present in this lead, while, at the same time, the precordial lead showed high, peaked T waves with little S-T depression.

The terminal electrocardiographic tracings were highly characteristic in all experiments except Experiment 17. The common sequence of events consisted of disappearance of the P wave followed within one to ten minutes by intraventricular block and cardiac arrest or ventricular fibrillation. The latter arrhythmia was seen in six experiments. In Experiment 17, disappearance of the P wave took place eighty-six minutes before death, with a serum potassium level of 25 mg. per cent and a temperature of 41.2° C. The serum potassium level continued to rise in this experiment and the T wave became heightened; terminally, there was deep S-T depression with a biphasic T wave followed shortly by intraventricular

block and cardiac arrest. The serum potassium level, obtained fourteen minutes before death, was 39 mg. per cent.

The serum potassium values and temperatures at which disappearance of the P wave took place are shown in Table I. As cardiac arrest followed so quickly the loss of the P wave, it was not always possible to obtain samples at that time. Accordingly, the table presents the last potassium value obtained prior to the disappearance of the P wave and also the interval elapsing between this sampling and the disappearance of the P wave.

Post-mortem serum potassium levels, obtained from the right ventricle as soon as possible after cessation of the heart beat, are also shown in Table I. As may be noted, there were pronounced post-mortem potassium increments in some experiments, whereas in others the post-mortem levels were the same or very near the levels of the final sample obtained from the living animal.

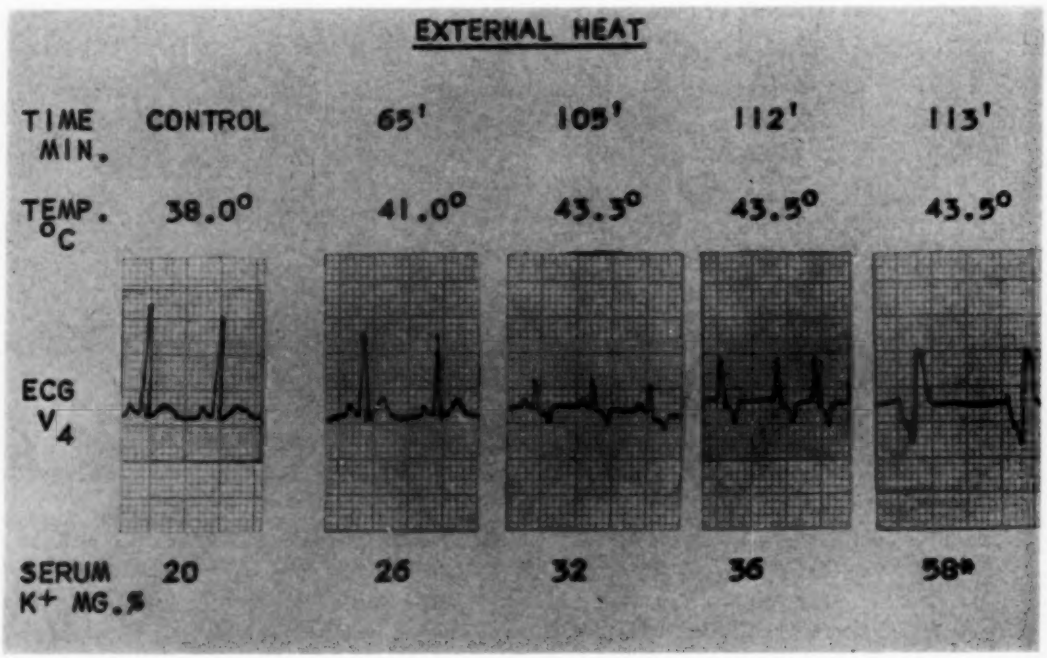


Fig. 2.—Progressive effects of external heat. Conditions as in Fig. 1.

In the experiments with external heat there was no apparent difference in results when the rate of hyperthermia was varied. Those animals which were heated quickly died at approximately the same temperatures and with similar potassium levels and electrocardiographic effects as those which were made hyperthermic over a much longer period.

Serum sodium levels were determined in thirteen experiments from the same samples from which potassium values were obtained. There was an average rise of about 5 per cent from control values averaging 330 mg. per cent. Serum calcium levels were determined in two dinitrophenol experiments. In one experiment the serum calcium values rose from 9 to 11 mg. per cent and in the other fell from 11 to 9 mg. per cent.

Serum hemoglobin determination made during the course of the calorigenic drug experiments indicated that the extent of hemolysis was negligible. In the external heat experiments there was an average increase in serum hemoglobin levels of 280 mg. per cent. Since most of the control whole blood potassium values were about 25 mg. per cent, hemolysis or leakage from the erythrocytes could not have contributed greatly to the high serum potassium levels.

Whole blood hemoglobin or hematocrit determinations, obtained in sixteen experiments, indicated that cell volume increased by about 10 per cent of control values in most experiments.

Venous oxygen contents determined frequently during the course of nine external heat experiments and six of the experiments with calorigenic drugs reflected the known difference in oxygen consumption produced by the two methods of hyperthermia.[12] With the calorigenic drugs, the oxygen content had dropped to levels less than 50 per cent of control values at the time the temperature reached 40° C. and continued progressively downward until extremely low levels were reached. In some experiments venous oxygen contents of less than 1 volume per cent were recorded. With external heat, the venous oxygen content remained near control values when the temperature reached 40° C. and did not drop significantly until the final stages of the experiments. Arterial oxygen content remained relatively stable with both types of hyperthermia. Respiratory failure preceded the onset of the final cardiac arrhythmias in most experiments, but this event should not have influenced the arterial blood oxygen saturation since artificial respiration with oxygen was maintained throughout.

Contractile force determinations demonstrated increments in contractile force, the average maximum determination reaching 180 per cent of the control level. This increase in contractile force produced by hyperthermia has been described in the previous report.[1] In most experiments the contractile force retained about 70 per cent of its control values at the time the terminal arrhythmias began and in two experiments the contractile force at this time was 100 per cent and 135 per cent of control.

Carotid pulse pressure measurements with the Statham Transducer demonstrated similar changes with both types of hyperthermia. The diastolic pressure usually began to drop at about 42.5° C. and continued precipitously downward until, at the time of the final arrhythmias, the diastolic pressure was only 20 to 30 mm. Hg. The run-off phase of the pressure pulse contour usually took on a shortened appearance prior to the onset of diastolic hypotension and became markedly shortened as the temperature continued to rise. Similar changes in pressure pulse contour have been reported by Wiggers and Orias[13] in radiothermia experiments. Synchronous contractile force and pressure pulse recordings from a typical experiment with external heat are shown in Fig. 3 with correlated temperature and electrocardiographic changes.

Maximal thoracic aortic compression late in the course of two experiments with Dicumarol when the diastolic pressures were 20 and 40 mm. Hg, respectively, and the temperatures 44° C. raised the diastolic pressure to about 100 mm. Hg in each case and maintained those levels for about five minutes, after which time the diastolic pressure again began to drop precipitously. This procedure did not alter the electrocardiographic changes which were present.

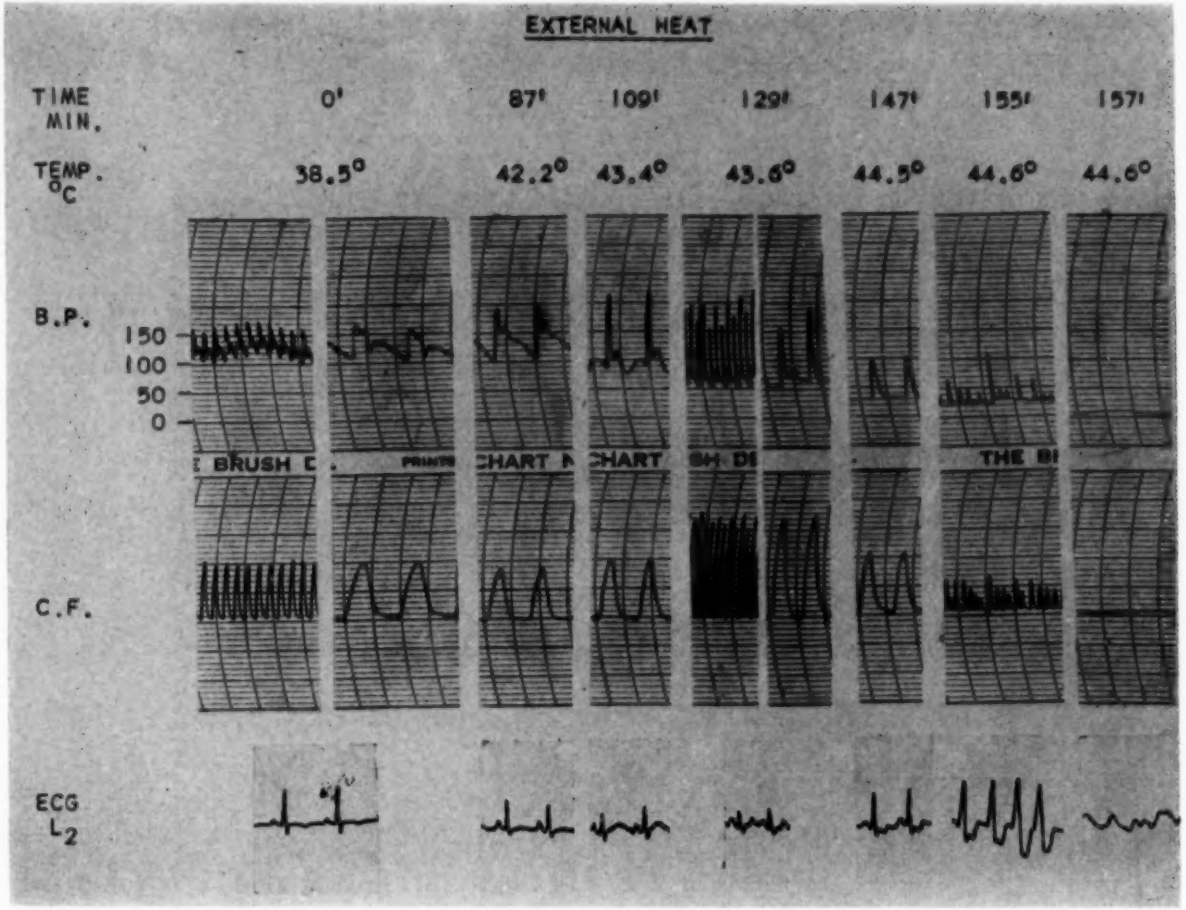


Fig. 3.—Synchronous oscillograph recordings of carotid pulse pressure (*B. P.*) and heart contractile force (*C. F.*) in an anesthetized dog made hyperthermic by external heat application. Two oscillograph speeds are shown, 5 mm./sec. and 25 mm./sec. Scale to the left of the *B. P.* recordings is in mm. Hg. Below the oscillograph recordings are correlated electrocardiographic tracings (Lead II).

The amplitude of oscillograph lever excursion is directly proportional to the systolic force acting against the two ends of a strain gauge arch which had been stitched to the anterior aspect of the right ventricle. In all such experiments measuring contractile force, the experiments were conducted on the first postoperative day.

The pH determinations in one experiment with Dicumarol and one with external heat demonstrated that the pH dropped to levels of about 7.1 from controls of about 7.3. Similar degrees of acidosis have been reported in the terminal stages of dinitrophenol intoxication by Hall and associates[12] and with hyperthermia produced by external heat by Hall and Wakefield.[14]

The three experiments with Tromexan demonstrated that hyperthermia could be produced by that drug in the dog. Temperatures at death were 41.2, 42.7, and 42.4° C. Tromexan differed from Dicumarol and dinitrophenol in that it produced a profound hypotension during the infusion period which necessitated a slow, divided administration. Gruber and associates[15] had previously reported that Tromexan resembled dinitrophenol in the rabbit in that it produced cyanosis and skeletal muscle and heart rigor. However, no hyperthermia was observed in their experiments.

DISCUSSION

These experiments have demonstrated that serum potassium levels of dogs made hyperthermic by calorigenic drugs or by external heat applications rise progressively to critically high levels. The electrocardiographic changes taking place in the experiments appear to be largely the result of the high serum potassium levels. The terminal electrocardiographic changes occurred at serum potassium levels somewhat lower than those originally reported with intravenous infusions of potassium salts by Winkler, Hoff, and Smith[16] but agreed more closely with the results of the recent infusion studies of Huggins and associates.[17,18]

The electrocardiogram correlated reliably with the rising serum potassium levels in most experiments. In only three experiments did the typical T-wave changes fail to appear. Disappearance of the P wave and intraventricular block was recorded in all experiments.

The fact that serum potassium increments and electrocardiographic changes took place at closely similar temperatures with the two types of hyperthermia appears to indicate that the serum potassium levels were more related to body temperature than to rate of metabolism. For it has been observed with dinitrophenol that oxygen consumption may double before the temperature rises and may reach levels ten times control in fatal intoxications,[12] whereas the oxygen consumption with physically induced hyperpyrexia has been generally found to follow van't Hoff's law in that oxygen consumption increases only two to three times with a 10° temperature rise.[19,20]

The following blood chemical determinations concomitantly obtained in these studies showed that secondary effects of hyperthermia were present which may have contributed to the high serum potassium levels, but which in themselves appear unlikely to have produced the total rise:

1. Acidosis, which was present in the latter stages of these experiments, as evidenced by pH values as low as 7.1, has recently been shown by Abrams, Lewis, and Bellet[21] to cause increments in plasma potassium levels. Those investigators produced metabolic acidosis in dogs by ammonium chloride administration until pH levels from 7.1 to 6.9 were reached. Plasma potassium levels

ends of a strain gauge arch which had been stitched to the anterior aspect of the right ventricle. In all such experiments measuring contractile force, the experiments were conducted on the first postoperative day.

were found to increase 11 to 13 per cent over control levels. Peaking of the T wave was the only consistent electrocardiographic change observed. Gertler, Hoff, and Humm[22] recorded similar T-wave changes in dogs killed by intravenous infusions of lactic and hydrochloric acids; the terminal electrocardiograms, however, did not resemble those produced by hyperpotassemia.

2. Although arterial oxygen levels were maintained near control values with both types of hyperthermia, the low venous oxygen contents observed indicate that some degree of tissue hypoxia was probably present. Mullen, Dennis, and Calvin[23] reported that asphyxia, produced in dogs by clamping the trachea, or hypoxia, produced by causing the animal to rebreathe in long tubes with removal of carbon dioxide by soda lime, produced serum potassium increments averaging 30 per cent of the control values. Wener and associates[24] reported that serum potassium levels of rabbits killed by pentobarbital or by clamping the trachea did not cause values to rise sufficiently high to cause terminal hyperpotassemic electrocardiographic changes, although the early T-wave changes did occur. Similar electrocardiographic results have been observed in these laboratories in dogs killed by anoxia and pentobarbital.[25,26]

3. Hemoconcentration, serum sodium, and serum calcium levels did not show sufficient change to have greatly influenced the sequence of events.

According to investigations of Daily and Harrison[27] and Prec and associates[28] the most important factor in hyperthermic death is peripheral vascular collapse. The present study does not directly contradict these results for, although the terminal arrhythmias appear to be due to hyperpotassemia, they took place, in most instances, in the presence of extreme hypotension (Fig. 3). It is possible that the lowered arterial pressure was responsible for some of the late rise in serum potassium levels by causing a diminished filtration pressure in the kidney.

Contractile force studies indicated that the force of the heart did not decrease to critically low levels, despite the marked drop in arterial pressure, until the time of occurrence of the final arrhythmias.

SUMMARY AND CONCLUSIONS

1. With anesthetized dogs under artificial respiration, serum potassium values rise to high levels during fatal hyperthermia.

2. The electrocardiographic changes occurring during hyperthermia can be largely explained on the basis of high serum potassium values.

3. The electrocardiographic and serum potassium changes produced by hyperthermia are basically similar regardless of whether the hyperthermia is produced by external heat or by the calorigenic drugs, Dicumarol and dinitrophenol.

4. Although serum potassium levels are sufficiently high to constitute the major cause of death under these conditions, other factors, particularly peripheral vascular collapse, may also be critical.

The frequent advice of Drs. W. M. McCord and P. C. Gazes is gratefully acknowledged, as is also the assistance of Miss Caroline James, Department of Medicine, in conducting a number of the manometric oxygen determinations.

REFERENCES

1. Walton, R. P., Goldberg, L. I., Gazes, P. C., Leary, J. S., Ezell, H. K., Hanna, C. B., and Prystowsky, R. P.: Effects of Hyperpyrexia on the Heart in Situ: A Study of Dicumarol, Dinitrophenol and External Heat, Am. J. Physiol. **169**:78, 1952.
2. Carlson, R. M., and Seager, L. D.: The Acute Toxic Effects of Dicumarol, Federation Proc. **7**:210, 1948.
3. Lequime, J., and Denolin, H.: Modifications circulatoires chez le chien au cours de l'hyperthermie produits par injection intra-musculaire de 2-4 dinitrophénate de sodium, Acta. brev. Neerland **12**:3, 1942.
4. Brewer, G.: The Relation of Plasma Potassium Level to Metabolic Activity, Am. J. Physiol. **129**:245, 1940.
5. Cheer, S. N.: The Effects of High Temperature on the Heart and Circulation in Intact Animals, Am. J. Physiol. **84**:587, 1928.
6. Giovanni, M.: Il compartamento dell'elettrocardiogramma nel colpo di calore provocato sul coniglio, Riv. di pat. sper. **7**:121, 1937.
7. Roos, A., Weisiger, J. R., and Moritz, A. R.: Studies on Thermal Injury. VII. Physiological Mechanisms Responsible for Death During Cutaneous Exposure to Excessive Heat, J. Clin. Investigation **26**:505, 1947.
8. Levine, H. D., Merrill, J. P., and Somerville, W.: Advanced Disturbance of the Cardiac Mechanism in Potassium Intoxication in Man, Circulation **3**:889, 1951.
9. Merrill, A. J.: The Significance of the Electrocardiogram in Electrolyte Disturbances, Am. Heart J. **43**:634, 1952.
10. Walton, R. P., Cotten, M. deV., Brill, H. H., and Gazes, P. C.: Factors Influencing Measurement of Contractile Force of Heart Muscle in Situ, Am. J. Physiol. **161**:489, 1950.
11. Finch, C. A., Sawyer, C. G., and Flynn, J. M.: Clinical Syndrome of Potassium Intoxication, Am. J. Med. **1**:337, 1946.
12. Hall, V. E., Field, J., 2nd, Sahyun, M., Cutting, W. C., and Tainter, M. L.: Carbohydrate Metabolism, Respiration and Circulation in Animals With Basal Metabolism Heightened by Dinitrophenol, Am. J. Physiol. **106**:432, 1933.
13. Wiggers, C. J., and Orias, O.: The Circulatory Changes During Hyperthermia Produced by Short Radio Waves (Radiothermia), Am. J. Physiol. **100**:614, 1932.
14. Hall, W. W., and Wakefield, E. G.: A Study of Experimental Heat-Stroke, J. A. M. A. **89**:177, 1927.
15. Gruber, C. M., Jr., Lee, K. S., Lasziczenko, Z. T., and Gruber, C. M.: A Study of the Toxicology and the Anti-Coagulant Action of Tromexan, a Synthetic Coumarin, Arch. internat. pharmacodyn. **87**:402, 1951.
16. Winkler, A. W., Hoff, H. E., and Smith, P. K.: Electrocardiographic Changes and Concentrations of Potassium in Serum Following Intravenous Injection of Potassium Chloride, Am. J. Physiol. **124**:478, 1938.
17. Huggins, R. A., Breckenridge, C. G., and Hoff, H. E.: Volume of Distribution of Potassium and Its Alteration by Sympatholytic and Antihistaminic Drugs, Am. J. Physiol. **163**:153, 1950.
18. Huggins, R. A., Seibert, R. A., and Bryan, A. R.: A Comparison of Effects of Morphine and Barbital on Volume Distribution of Potassium, Am. J. Physiol. **168**:33, 1952.
19. Nasset, E. S., Bishop, F. W., and Warren, S. L.: Physiological Effects of High Frequency Current. I. Respiratory Metabolism and Certain Changes in the Blood of Anesthetised Dogs, Am. J. Physiol. **96**:439, 1931.
20. Nasset, E. S.: Physiological Effects of High Frequency Current. II. Further Studies on Respiratory Metabolism of Anesthetised Dogs, Am. J. Physiol. **101**:194, 1932.
21. Abrams, W. B., Lewis, D. W., and Bellet, S.: The Effect of Acidosis and Alkalosis on the Plasma Potassium Concentration and the Electrocardiogram of Normal and Potassium Depleted Dogs, Am. J. M. Sc. **222**:506, 1951.
22. Gertler, M. M., Hoff, H. E., and Humm, D. G.: The Acid Tolerance of the Dog Heart, Am. J. Physiol. **146**:478, 1946.
23. Mullin, F. J., Dennis, J., and Calvin, D. B.: Blood Potassium in Tetany and Asphyxia of Dogs, Am. J. Physiol. **124**:192, 1938.
24. Wener, J., Stansfield, H., Hoff, H. E., and Winter, H. A.: Potassium Autointoxication From Hemolysis of Red Cells, Am. Heart J. **37**:881, 1949.
25. Boniface, K. J., Brown, J. M., and Ferrara, E.: The Influence of Carbon Dioxide, Anoxia and Asphyxia on the Contractile Force of the Heart (Dog), J. Pharmacol. & Exper. Therap. **101**:3, 1951.
26. Boniface, K. J., and Brown, J. M.: Elevation of the Cardiac Depressant Dose of a Barbiturate With Cardiac Stimulant Drugs, Federation Proc. **11**:324, 1952.
27. Daily, W. M., and Harrison, T. R.: A Study of the Mechanisms and Treatment of Experimental Heat Pyrexia, Am. J. M. Sc. **215**:42, 1948.
28. Prec, O., Rosenman, R., Braun, K., Harris, R., Rodbard, S., and Katz, L. N.: The Circulatory Responses to Hyperthermia Induced by Radiant Heat, J. Clin. Investigation **28**:301, 1949.

THE RELATIONSHIP OF SOME ELECTROLYTES OF THE SERUM, EDEMA FLUID, AND URINE IN A CASE OF INTRACTABLE HEART FAILURE

LOUIS A. SOLOFF, M.D., JACOB ZATUCHNI, A.B., M.S., M.D., AND JOSEPH H. BOUTWELL, M.S., PH.D., M.D.

PHILADELPHIA, PA.

THE EDEMA of cardiac failure is almost universally regarded as an ultrafiltrate derived from plasma.[1] The slight differences in electrolyte concentration in plasma and in edema fluid is explained by Donnan's equilibrium theory because of the differences in protein content of these compartments.[2] The determination of extracellular sodium is based upon this assumption. Thus, such a determination merely requires that one measure the concentration of sodium in the plasma and multiply this amount by the (estimated) volume of extracellular fluid.

We have recently had the opportunity for measuring the intake and urinary output and the concentrations in plasma and in edema fluid of sodium and potassium daily for thirty-six days in an individual with intractable heart failure.

The purpose of this report is to indicate that there may be large differences between the concentrations of sodium in the plasma and that of the edema fluid. These results suggest that dynamic changes occurring spontaneously or after therapy may alter the equilibrium between plasma and edema fluid and may be a factor in the persistence of heart failure.

CASE REPORT

H.S., a 50-year-old white man, first presented himself to the medical outpatient clinic of the Episcopal Hospital on March 25, 1950. He was perfectly well until October, 1948, when he experienced several episodes of precordial pain occurring on effort and relieved by rest. About two weeks later, while playing with his dog, he suddenly became dizzy and began to perspire profusely. A severe pain developed in the region of the upper midabdomen. He rushed into his house and called his doctor. The pain persisted until he received injections of morphine sulfate for its relief. He remained at bed rest at home for three weeks and then returned to work as a watchman at a factory.

He was apparently well until January, 1950, when he experienced on effort precordial aching pain accompanied by a sensation of tightness, which was relieved by rest. He noticed also that he was becoming increasingly short of breath on effort. In March, 1950, his ankles began to swell. Examination on March 25, 1950, revealed a blood pressure of 128/98 mm. Hg. The heart was enlarged to the left anterior axillary line and a Grade I precordial systolic murmur was present. The rhythm was regular. The lungs were clear. The liver was felt three fingerbreadths below

From the Department of Medicine and the Department of Chemistry, Temple University Medical School and Hospital, Philadelphia, Pa.

Received for publication Aug. 15, 1952.

the right costal margin in the midclavicular line. The cervical veins were distended and pitting edema of the lower extremities and scrotum was present. He weighed 165 pounds. He was digitalized and mercurial diuretics were administered. Limitation of activity and restriction of salt intake were advised.

He continued to attend the medical clinic during the ensuing months at frequent intervals. The serologic tests for syphilis were negative. A fasting blood sugar was 124 mg. per cent. A hemogram and urinalysis were normal. He apparently responded well to mercurials, for on April 6, 1950, he weighed 135½ pounds. His blood pressure was 112/78 mm. Hg. A chest roentgenogram indicated slight left ventricular enlargement. An electrocardiogram taken on April 6, 1950, revealed changes consistent with a diagnosis of old anterior and posterior myocardial infarctions and digitalis effect. Although he received injections of mercurial diuretics at weekly intervals, his weight gradually increased. He again experienced precordial or epigastric pain and shortness of breath on effort, and had orthopnea and ankle edema.

From Jan. 12, 1951, to Jan. 24, 1951, he was in the Episcopal Hospital for treatment of cardiac decompensation. An electrocardiogram and chest roentgenogram revealed no significant changes since the previous one. Roentgenographic study of the gastrointestinal tract, including a cholecystogram, was negative.

He attended the medical clinic and, later, the cardiac clinic, receiving his mercurial injections weekly. However, he continued to have repeated anginal attacks and shortness of breath. In the latter part of November, 1951, it was noticed that he was getting less and less of a diuretic response to mercurials in spite of progressive edema.

On Dec. 6, 1951, he was again admitted to the Episcopal Hospital. He was dyspneic and cyanotic. The cervical veins were distended. Blood pressure was 140/80 mm. Hg. The heart was enlarged to the left anterior axillary line. The rhythm was regular at 100 per minute. P_2 was greater than A_2. A precordial Grade III systolic murmur, loudest in the left fourth intercostal space parasternally, was present. The lungs were clear. The liver edge was again palpated three fingerbreadths below the right costal margin in the midclavicular line. There was shifting abdominal dullness and pitting edema of the lower extremities. The venous pressure was 260 mm. of water. The ether time was 5 seconds and the Decholin time was 55 seconds. Mercurials were given daily but there was no diuretic response. The urinary output remained below 1,000 c.c. daily. Digitoxin, (0.2 mg. daily), was continued. On Dec. 8, 1951, he was given an additional 0.2 mg. dose of digitoxin. On Dec. 12, 1951, a bigeminal rhythm was present. An electrocardiogram revealed a sinus rhythm with multifocal ventricular beats occurring in bigeminus; otherwise, there was no significant change from the previous tracings. Digitoxin was discontinued. The intravenous administration of Pronestyl Hydrochloride, (100 mg.), resulted in a prompt disappearance of the ectopic beats. Pronestyl Hydrochloride was then given orally (500 mg. four times daily). However, nausea and vomiting developed and persisted in spite of decreasing the dosage of Pronestyl (250 mg. four times daily). Premature beats reappeared. Examinations repeated daily revealed periods of regular rhythm and periods of bigeminus. Occasionally, simply by the changing of his position from either erect to supine or vice versa a sinus rhythm was converted to bigeminus. Potassium chloride, 1 Gm. in 180 c.c. orange juice four times daily, did not alter the arrhythmia. He was again given digitoxin, (0.2 mg. daily), from Dec. 21, 1951, to Dec. 26, 1951, with no effect. The response to various measures during a prolonged balance study is indicated in Fig. 1. He continued to have massive edema with involvement of the scrotum and penis and became progressively lethargic. Although he was dyspneic at rest, it was not marked. The cervical veins remained distended. The lungs were clear. On Jan. 12, 1952, he developed a sharp pain in the left anterolateral hemithorax accompanied by cough productive of white phlegm and of bright red blood. Examination of the lungs remained negative. On Jan. 22, 1952, he suddenly cried out, complaining of pain in the left chest. He developed pulmonary edema and died in a few minutes.

Autopsy, performed by Dr. Harvey Watts, revealed fibrosis at the apex of the heart and on the posterior wall of the left ventricle. A pulmonary infarction was present in the left lower lobe.

DISCUSSION

Some of the causes of intractable heart failure have been reviewed recently.[3,4] In brief, they may be divided into: (1) incorrect diagnosis, (2) unrecognized associated illnesses, (3) diseases which secondarily overburden the heart and which are as yet unamenable to therapy, (4) under- or over-treatment, (5) unavoidable (?) side effects of treatment, (6) nutritional disturbances which produce abnormal quantitative or qualitative metabolic disturbances, or any combination of these causes.

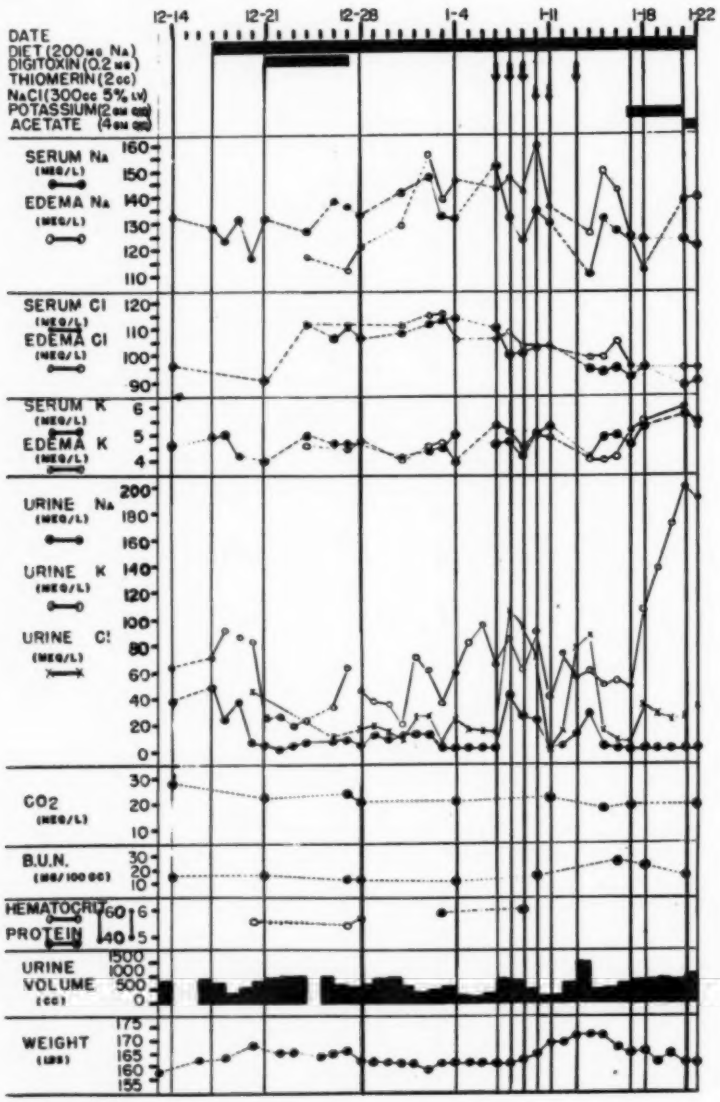


Fig. 1.—The relationship of the concentrations of sodium, potassium, and chloride in the serum to that of the edema fluid and urine in Patient H.S. while on a constant dietary intake.

The morbid anatomist can recognize the first three. He cannot as yet diagnose the others. This is one of the reasons why the pathologist cannot at all times distinguish the heart removed from an individual who died of heart failure from one who died of another cause. For this same reason, the clinician cannot be certain that the myocardium has reached its intrinsic limit of adequate contraction.

It appears to us that unavoidable (?) side effects of treatment and nutritional disturbances were at least significant contributory causes of intractable heart failure in our patient.

The initial determinations of serum and urinary concentrations of sodium were below normal. With a decrease in the daily dietary sodium to 8.7 meq., the urinary sodium concentration decreased within three days to values less than 10 meq./L., a response considered by Newburgh[5] to be that of normal renal tubular function. At no time was renal impairment of function diagnosed. On the contrary, the decreased sodium intake was accompanied by a gradually increasing serum concentration of sodium. The serum sodium concentration was higher than that of the edema fluid and on one occasion by as much as 24 meq./L. This difference is a significant one in our laboratory.

It is tempting to theorize on the influence of such concentrations and differences in concentration on urinary flow and consequently on the manifestations of heart failure. The increasing sodium concentration in the serum was not accompanied by any change in hematocrit, body weight, or other clinical manifestations. Yet profound electrolyte shifts at the cellular level must have occurred, for if the average loss of sweat and fecal sodium is 10 meq. per day, it would appear that the patient was in a slightly negative sodium balance in contrast to the positive potassium balance as indicated by an intake of 96.2 meq. and an average urinary loss of less than 50 meq. per day. Nevertheless, the potassium concentrations in the serum and edema fluid remained relatively constant. It would appear, therefore, that sodium was leaving the cells of the body and potassium was entering them.

When the serum sodium concentration was 152 meq./L., an intramuscular injection of Thiomerin, (2 c.c.), produced a marked excretion of chloride, a moderate excretion of sodium, and a slight excretion of potassium. The serum concentrations of chloride and of sodium dropped markedly without any change in the edema fluid concentrations of these electrolytes. Following repeated injections of Thiomerin, the difference of the concentrations of sodium in the edema fluid and plasma increased and on one occasion by as much as 25 meq./L. The urinary volume remained low and the patient gained weight.

This state resembled the low-sodium, low-chloride syndrome.[6] Hence, 5 per cent sodium chloride, (300 c.c.), was given intravenously. During its administration, there occurred a visible decrease in edema. However, it was evanescent. The patient became thirsty and was relieved by drinking water, indicating a state of relative dehydration. The urinary volume decreased, the body weight increased, and the serum and urinary sodium concentrations decreased. Similar results occurred on the following day when a hypertonic sodium chloride solution again was given intravenously.

Potassium acetate was then administered with the hope that a latent potassium deficit might be contributing to the intractable failure.[7] Support was given to this thought by experience with other instances of heart failure and by the recurrent bigeminal rhythm. The exhibition of potassium produced a tremendous outpouring of potassium in the urine in a quantity nearly equivalent to the intake. The urinary volume remained low in spite of the high concentrations of potassium in the serum and in the urine.

At autopsy, heart muscle blocks from the left ventricle and skeletal muscle blocks from the intercostal muscles were obtained. Fibrous and fatty tissues were carefully dissected away. The fluid content was determined by weighing before and after dessication at 105° F. to constant weight. The electrolyte concentrations which are shown below were determined on another wet sample after extraction with 0.75N nitric acid for two days.[8]

	SODIUM	POTASSIUM	CHLORIDE	DRY SOLIDS
	MEQ. / KG. WET TISSUE			(%)
Cardiac muscle	57.5	52.5	36.6	18.8
Intercostal muscle	30.8	104.6	23.4	23.6

It would appear that the negative sodium balance and positive potassium balance were reflected in the skeletal muscle concentrations of these electrolytes: the sodium concentration was decreased and the potassium concentration was increased. However, in the heart muscle, significantly decreased concentrations of sodium and potassium were exhibited.

The changes in electrolyte concentration which have been described are not necessarily characteristic of those occurring in others with intractable heart failure.[9] To be sure, the syndrome of intractable heart failure has certain common features clinically. But, many of these occur in association with diseases other than those of the heart and present difficulties in diagnosis which confound the clinician. Furthermore, different types of heart disease may be associated with different myocardial metabolic disturbances leading to failure.[10] From the clinical standpoint, heart failure is the inability of the heart to transfer blood from the venous to the arterial side and results from either a decreased efficiency or an increased load or both.

The findings reported herein indicate that there may be differences in the sodium content of edema and plasma fluid which may be spontaneous or induced by therapy. It would appear to us, therefore, that these changes may be related to metabolic derangements of the peripheral tissues and may have some significance in the intensification and persistence of cardiac failure.

SUMMARY

An individual with intractable heart failure and with normally functioning kidneys died on the thirty-ninth day of hospitalization. During this time, his

diet was fairly uniform and constant for sodium and potassium. Daily records were made of the weight and fluid balance, of the concentration of sodium, potassium, and chloride, of plasma and edema fluid, and of the total output of these electrolytes in the urine. The effect was noted on these determinations of: (1) no medication, (2) digitoxin, (3) mercurials, (4) hypertonic salt solution, and (5) potassium acetate. In the untreated state, the serum sodium was significantly higher than that of the edema fluid. This relationship could be temporarily reversed by mercurials that caused a sharp increase in urinary sodium and chloride. Oral potassium was excreted almost quantitatively in the urine. Hypertonic salt solution and digitoxin were without appreciable effect. The individual variability of the manifestation of cardiac failure, a gradient of sodium between plasma and edema fluid, is reported.

REFERENCES

1. Friedberg, C. K.: Electrolyte and Fluid Disturbances in Congestive Heart Failure, New England J. Med. **245**:812, 1951.
2. Gamble, J. L.: Chemical Anatomy, Physiology, and Pathology of Extracellular Fluid. A Lecture Syllabus, Cambridge, 1949, Harvard University Press.
3. Soloff, L. A.: Some Clinical Aspects of Refractory Heart Failure, Mod. Concepts Cardiovas. Dis. **19**:73, 1950.
4. Proger, S., and O'Connor, J. J.: Intractable Heart Failure, Ann. Int. Med. **33**:1349, 1950.
5. Newburgh, L. H.: Significance of the Body Fluids in Clinical Medicine, Springfield, Ill., 1950, Charles C Thomas, Publisher.
6. Soloff, L. A., and Zatuchni, J.: Syndrome of Salt Depletion. Induced by a Regimen of Sodium Restriction and Sodium Diuresis, J. A. M. A. **139**:1136, 1949.
7. Fox, C. L., Jr., Friedberg, C. K., and White, A. G.: Electrolyte Abnormalities in Chronic Congestive Heart Failure: Effect of Administration of Potassium and Sodium Salt, J. Clin. Investigation **28**:781, 1949.
8. Lowry, O. H., and Hastings, A. B.: Histochemical Changes Associated With Aging. I. Methods and Calculations, J. Biol. Chem. **143**:257, 1942.
9. Elkinton, J. R., and Squires, R. D.: The Distribution of Body Fluids in Congestive Heart Failure. Theoretic Considerations, Circulation **4**:579, 1951.
10. Olson, R. E., and Schwartz, W. B.: Myocardial Metabolism in Congestive Heart Failure, Medicine **30**:21, 1951.

REVASCULARIZATION OF THE HEART. OBSERVATIONS ON THE CIRCULATION FOLLOWING ARTERIALIZATION OF THE CORONARY SINUS

RICHARD S. HAHN, M.D.,* MAURICE KIM, M.D.,** AND CLAUDE S. BECK, M.D.***

CLEVELAND, OHIO

DURING the past six years a full-time investigation was carried out in this laboratory in an attempt to provide the heart muscle with an additional supply of red blood. The method used was the placement of a free graft of jugular vein between aorta and coronary sinus.[1,2,3] For this method to be successful it was found that the operation must be done as a two-stage procedure.[4] The first stage consisted in placement of the graft. The second stage was done several weeks after the first and consisted in partial ligation of the coronary sinus at its ostium in the right auricle so that all of the blood did not escape into the auricle. Following this two-stage operation it was possible to ligate the descending ramus of the left coronary artery at its origin in one step with a reduction in mortality and with a reduction in destruction of heart muscle as compared to the mortality and infarction in normal unprotected hearts (Table I). It was also possible to ligate this artery without the usual electrocardiographic changes that are found in a normal unprotected heart.[7] Complete ligation of descending ramus, circumflex ramus, and right coronary arteries were accomplished with recovery of dogs and with only slight damage to the myocardium. Only the septal branch of the left coronary artery was patent in these experiments.[6]

In order to explain this reduction in both mortality and infarction the assumption was made that blood flowed from the aorta through the graft, into the coronary sinus and its tributaries. From these veins it was assumed that aortic blood traversed the capillary bed where oxygen exchange was possible. No other explanation for this protection seemed to be possible. However, to some interested in this development, this protection did not seem to be adequate proof that this blood did traverse the capillary bed. Additional evidence appeared to be necessary. Direct proof of this assumption was not possible to obtain. This would require a segregated venous inflow, a segregated myocardial capillary bed, and a segregated arterial exit. This was not possible in the heart, but re-

From the Laboratory of Cardiovascular Research, Western Reserve University and the University Hospitals, 2065 Adelbert Road, Cleveland 6, Ohio.

This work was supported by grants from the United States Public Health Service and the Cleveland Area Heart Society.

Received for publication April 25, 1952.

*Research Fellow, United States Public Health Service.

**Fulbright Exchange Fellow, University Hospital, Strasbourg, France.

***Professor of Cardiovascular Surgery, Western Reserve University.

cently it was proved that blood could flow in a retrograde direction in a segment of isolated bowel where all three of these factors were controlled.[8] In these experiments arterial blood gave up its oxygen.

TABLE I. LIGATION DESCENDING RAMUS LEFT CORONARY ARTERY

NORMAL DOGS[5]

NUMBER	LIVING	DEAD
10	3	7
10	1	9
10	4	6
10	2	8
10	5	5
Total 50	15 (30%)	35 (70%)

GRAFT OCCLUDED BY THROMBOSIS[6]

NUMBER OF DOGS	LIVING	DEAD
10	3 (30%)	7 (70%)

GRAFT PATENT[1,4,8]

NUMBER OF DOGS	LIVING	DEAD
10	8	2
10	9	1
17	16	1
13*	6	7
Total 50	39 (78%)	11 (22%)

*These 13 experiments were done during a period of hot weather. Perhaps factors other than the ligation of the descending ramus determined this mortality.

METHOD OF STUDY

A segment of jugular vein was placed between the coronary sinus and the aorta. Several weeks later the coronary sinus was occluded to a diameter of 2 to 3 mm. at the ostium of the sinus into the right auricle. At this second operation the right coronary artery was totally occluded at its origin. Several weeks later a third operation was done. The common left coronary artery was dissected out together with the circumflex ramus. The circumflex ramus was ligated at its origin and this artery was cut distal to the ligature. The distal end was cannulated with a piece of polyethylene tubing. Heparin was given intravenously. Determinations of pressure, flow, and oxygen content were made on the blood

from the distal end of the severed artery over a period of several hours. These determinations were done with the graft carrying blood from the aorta and also with the graft occluded and not carrying blood from the aorta. Pressures were determined with the Sanborn electromanometer.

RESULTS

The results obtained in one of these experiments are shown in Table II. By reference to this table it will be seen that a large part of the coronary artery inflow was occluded during the course of this experiment. In the lowest box of the table the only arterial inflow was through a lumen of 0.5 mm. of the left common coronary artery. It will be noticed that the heart continued to beat over a three-hour period with the circumflex and the right coronary arteries completely occluded. This would probably not be possible in a normal unprotected heart. The pressures in the distal circumflex artery measured 50, 35, 50, and 42 mm. Hg with the graft open and carrying blood from the aorta. These pressures appeared to be maintained regardless of coronary artery inflow. Additional occlusion of arteries did not lower the pressure. With the graft closed off so that no blood came from the aorta by way of the graft these pressures measured 20, 12, 7, and 0 mm. Hg. These pressures were always at a lower level with the graft closed off as compared to the pressures with the graft open. The pressures fell progressively as coronary artery inflow became progressively reduced. The conclusions were reached that these arterial pressures were consistently higher with an open graft as compared to the figures obtained with a closed graft; that the pressures with an open graft remained on a higher level regardless of coronary artery inflow occlusion, and that the pressures with the graft closed off progressively fell as the amount of coronary artery occlusion was increased. The graft was effective in producing and maintaining arterial pressure distal to a complete occlusion of a major coronary artery, whereas without the graft the pressure distal to the occlusion was low and even low levels could not be maintained as arterial occlusion increased.

The backflow of blood per minute from the severed artery measured 6.0, 7.0, 13.5, and 12.5 c.c. with the graft open, and 4.0, 3.5, 3.0, and 2.0 c.c. with the graft closed off. The flow was uniformly greater with the graft open. Furthermore, the backflow increased as arterial inflow was reduced. The greatest backflow occurred when the arterial inflow was almost completely cut off.

The oxygen content of the retrograde blood had 2.3 volumes per cent with the graft open and 9.5 volumes per cent with the graft closed off. In all succeeding tests the blood was blue when the graft was open and it was noticeably pink when the graft was closed off. These alterations in color of the blood occurred within a few seconds after the graft was alternately opened and closed. Oxygen determinations in retrograde blood in another similar experiment showed 9.3 volumes per cent with the graft open and 15.4 volumes per cent with the graft closed off.

Similar results were obtained in other experiments. However, in two experiments the results were different. These experiments were done in the same way as in those recorded. The results obtained in one of these experiments are shown in Table III. As indicated in the first column of the table, the right coronary artery and the circumflex ramus of the left coronary artery were totally occluded. In addition to these arteries the left common coronary artery was occluded to a lumen of 1.5 mm. and the heart continued to beat. Finally this artery was completely occluded and the heart stopped within a few minutes. The pressures in the circumflex artery distal to the occlusion were somewhat lower with the graft closed off as compared to the pressures with the graft open. Only slight changes were found in flow with the graft open and closed. The blood was red with the graft open and closed, and the oxygen content showed only slight alteration.

TABLE II*

	TIME INTERVAL (HR.)	GRAFT FROM AORTA	DETERMINATIONS FROM DISTAL CUT END OF CIRCUMFLEX ARTERY		
			PRESSURE (mm. Hg.)	FLOW PER MINUTE (C.C.)	O_2 CONTENT OR COLOR OF BLOOD
Total occlusion right and circumflex arteries	None	Open	60/41 mean 50	6	2.3 vol. %
		Closed	24/12 mean 20	4	9.5 vol. %
	½	Open		7	Blue
		Closed		3.5	Red
Also occlusion left common artery to 2 mm.	1½	Open	41/30 mean 35	6	Blue
		Closed	16/9 mean 12	3.5	Red
	2½	Open	56/37 mean 50	13.5	Blue
		Closed	15/6 mean 7	3	Red
Also occlusion left common artery to 0.5 mm.	3	Open	50/30 mean 42	12.5	Blue
		Closed	None	2	Red

*A segment of jugular vein was placed between aorta and coronary sinus. Three weeks later the coronary sinus was ligated at its ostium to a diameter of 3 mm. and the right coronary artery was completely occluded at its origin at this same operation. Several weeks later the left common coronary artery with the circumflex ramus was dissected out. The circumflex ramus was ligated and its distal end was cannulated. The common left coronary artery was then further occluded. Pressure, flow, and oxygen content or color of blood from the distal end of the circumflex artery are recorded with the graft open and closed.

DISCUSSION OF RESULTS IN TABLE II

These experiments provided several points for discussion. In the first place, the graft almost certainly protected the heart so that such extensive occlusion of coronary arteries could be done with maintenance of the heart beat for a period of three hours. In the second place the graft was effective in maintaining pressure in a major artery distal to a complete occlusion. It was effective in maintaining pressure regardless of the extent of the occlusive process in the arteries. Indeed,

the experiments showed that the flow from the severed artery increased as the occlusive process in the arteries was increased. It would appear that the greater the occlusion in the other coronary arteries the greater was the amount of blood in the test artery beyond the ligature. Of greatest significance was the color of the retrograde blood. With the graft open the retrograde blood was blue and one oxygen content measured 2.3 volumes per cent. With the graft closed off the blood was pink and one oxygen content measured 9.5 volumes per cent. The change from blue to pink to blue was readily noticeable as the graft was closed, opened, and closed. The only explanation for this was that the blood was blue because it gave up its oxygen, and the only place where it could give up its oxygen was in the capillary bed where oxygen exchange was possible. This blue blood with the graft open must have been aortic blood that traversed the capillary bed where it gave up its oxygen. When the graft was shut off the blood was red. It was arterial blood. It did not go through a capillary bed. It was always small in amount and under low pressure. It must have come from other coronary arteries by way of intercoronary arteries.

TABLE III*

	GRAFT FROM AORTA	DETERMINATIONS FROM DISTAL END OF CIRCUMFLEX ARTERY		
		PRESSURE (mm. Hg.)	FLOW PER MINUTE (C.C.)	O_2 CONTENT OR COLOR OF BLOOD
Total occlusion right and circumflex arteries	Open	56/36 mean 50	6	22.0 vol. %
	Closed	38/32 mean 36	7.5	19.0 vol. %
Also occlusion left common artery to 1.5 mm.	Open	44/24 mean 36	3.5	Red
	Closed	32/16 mean 22	3	Red
Also occlusion left common artery complete	Open	57/27 mean 50	3	Red
	Closed	— —	—	Red

*A segment of jugular vein was placed between aorta and coronary sinus. Three weeks later the coronary sinus was ligated at its ostium to a diameter of 3 mm. and the right coronary artery was completely occluded at its origin at the same operation. Several weeks later the left common coronary artery with its circumflex ramus was dissected out. The circumflex ramus was ligated and its distal end was cannulated. The common left coronary artery was then further occluded. Pressure, flow, and oxygen content or color of blood from the distal end of the circumflex artery are recorded with the graft open and closed. The first sample of blood was taken immediately after the left common coronary artery and the circumflex coronary artery were dissected out and the circumflex artery was ligated and its distal end cannulated. The second sample was taken one hour later and the third sample was taken three hours after the first. The third specimen was taken after all coronary arteries were occluded and just before the heart stopped beating.

DISCUSSION OF RESULTS IN TABLE III

In these experiments there was no evidence that blood flowed from the graft through the capillary bed and escaped from the severed artery. There can be little doubt that the heart in each of these experiments was a protected heart, otherwise such extensive ligation of coronary arteries with maintenance of the heart beat probably would not have been possible. Explanation for the protection can only be theoretical. Perhaps the assumption can be made that arterial blood entered the capillary bed and escaped freely into the rich network of venous channels that are present in the myocardium without entering the severed artery. If this assumption were correct it would mean that arterial blood could enter the capillary bed by way of venous channels and also escape by way of venous channels without going all the way back into arterioles and finally into the major artery as occurred in experiments shown in Table I. These venous channels are shown in Fig. 1. The backflow through the severed artery was arterial blood and no doubt came from intercoronary channels, but the evidence is scarcely adequate to indicate that an augmentation of these channels was brought about by this two-stage operation. More recently it was shown by Eckstein and colleagues that this operation produced two types of result. One was actual backflow from the aorta and the other was the development of intercoronary arterial communications.

The coronary veins of the left ventricle consist of a rich interlocking system as compared to the arteries. Fig. 1, *C* and *D*, shows an erosive specimen of arteries and veins in the left ventricle. The veins are many times more numerous than are the arteries and the communications between veins are much more numerous than are the communications between coronary arteries. If one accepts the possibility of retrograde flow in the venous system it can be readily seen that ischemic areas of myocardium are less likely to develop in such a rich interlocking system of veins. From the standpoint of anatomy it should be readily possible for blood to reach practically any area of the left ventricular myocardium. In contrast to this is the sparsely interlocking system of coronary arteries which allows ischemic areas or trigger areas to develop and which in turn so frequently produce ventricular fibrillation and death. Indeed, the benefit of the two-stage operation may be due in part to a supporting action, so to speak, to the ischemic area produced by major artery occlusion. A small amount of oxygenated blood delivered to ischemic muscle can reduce the destruction of muscle fibers and can also reduce the incidence of ventricular fibrillation. If this supporting action can preserve the heart beat over the crisis of an arterial occlusion, then the time factor adds additional support to the heart beat. This additional aid consists of intercoronary arterial channels. These channels can develop in a matter of days after an artery has been occluded.

Gregg and his associates[9,10] have done flow studies after ligation of the coronary sinus and also after ligation and section of the descending ramus of the left coronary artery. In experiments in which this artery was ligated and cut and without ligation of the sinus the retrograde flow was arterial but consisted

of only a few cubic centimeters per minute. Several weeks after this artery was ligated the retrograde flow increased to 12 to 15 c.c. per minute. In each instance this was arterial blood and came from intercoronary arterial channels. The amount of intercoronary arterial flow was increased because these channels between arteries increased in size and number after one of the arteries was ligated. The time factor is necessary for this development to take place. If the coronary sinus were ligated first and then the descending ramus of the left coronary artery was ligated and cut, then the backflow from the cut artery rose to values as high as 39 to 40 c.c. per minute and this blood was venous and showed oxygen values of 2 to 4 volumes per cent. These authors expressed some doubt about the origin of this backflow. They found that if the circumflex ramus of the left coronary artery was ligated also, then the amount of backflow fell off appreciably. A possible explanation was that blood from the circumflex artery traversed the capillary bed and entered the coronary sinus. From the coronary sinus it returned by way of sinus tributaries in a retrograde direction through the capillary bed of the descending ramus and emerged from the cut end of this artery. According to this explanation the blood traversed two capillary beds in order to escape from this artery. It traversed the capillary bed of the intact circumflex artery and returned in a retrograde direction through the capillary bed of the descending artery and escaped from this cut artery. This blood had very little oxygen left in it.

OTHER OBSERVATIONS

The two-stage operation was done in a large number of experiments and a major coronary artery was ligated at a subsequent operation. In many of these experiments we observed the artery distal to the ligature take on a bluish color within a few seconds after the artery was ligated. After the artery was cut the blood from the artery appeared to be reduced venous blood. It was also observed that after the artery was cut and blood was allowed to escape from the distal cut end of the artery that the heart beat became weak and the electrocardiogram showed further evidence of ischemia. It appeared that this blood in the artery distal to the occlusion was serving a useful purpose.

Fig. 1.—*A* and *B*, A graft of jugular vein was placed between aorta and coronary sinus. Three weeks later the coronary sinus was partially ligated at its ostium in the right auricle. Three weeks later the descending ramus of the left coronary artery was totally occluded at its origin in one step. The dog was killed five months later. A mixture of barium chloride and gelatin was injected into the graft and coronary arteries. The white mixture was injected into the graft and the pink mixture was injected into the circumflex ramus of the left coronary artery. This mixture is too thick to penetrate the capillary bed. Photograph at upper left shows aorta, graft, and coronary sinus and its tributaries in white. In *B* the circumflex artery can be identified by the loop of black silk. This artery contains both pink and white material. In *A* the magna cordis vein is white. This is a tributary of the coronary sinus. The descending coronary artery can be identified by the loop of black silk. On each side of this artery is a vein. One vein is pink and one is white. The ligated artery is white. This artery filled from the veins. The pink vein filled from the circumflex artery. Direct communications between arteries and veins and between veins and arteries can be traced without the interposition of a capillary bed.

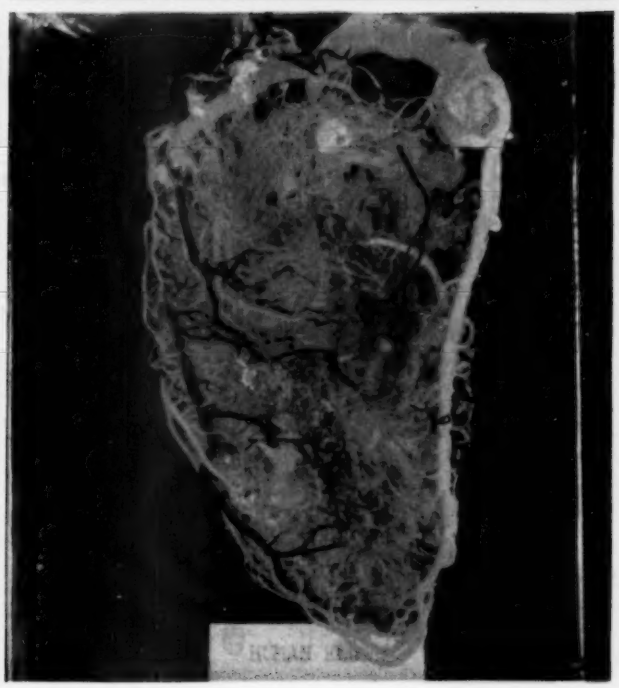
***C* and *D* are photographs of a human heart. The coronary sinus and the left coronary artery were injected with Vinylite. The sinus was injected with yellow material and the artery was injected with pink. The muscle was dissolved in sodium hydroxide. Photograph on left (*C*) shows the appearance from the surface of the left ventricle; the photograph on the right (*D*) shows the appearance from the cavity of the left ventricle. Note the difference in the arterial and venous beds. The venous bed is much richer than the arterial bed and the veins communicate freely with each other. (Vinylite is made by the Bakelite Division of the Union Carbide and Carbon Corporation, 30 East 42nd Street, New York, N. Y.)**

AM. HEART J.
Vol. 44, No. 5, Nov., 1952

A

B

C



D

(For legend, see opposite page.)

Several confirmatory observations were made in human patients in whom this operation was done for coronary artery disease. In these patients with arterial disease, backflow of arterial blood took place in the venous system more readily than was observed in dogs with normal coronary arteries. In these patients after the graft was placed between aorta and coronary sinus and after the sinus was partially occluded at its ostium, the veins of the left ventricle became bright pink and the myocardium became pink. The following observation was made in several patients. At the second stage of the operation the parietal pericardium was adherent to the heart. The parietal pericardium was separated from the heart and bleeding occurred from many small points where adhesions were broken. Thus an oozing surface was created and as one observed this surface some drops of blood, as they gradually formed, were blue and others were pink. This blood became uniformly bright pink immediately after the sinus was ligated and for several minutes the amount of oozing was increased. There was no trace of venous color in the blood on this oozing surface. The origin of the blood from the oozing surface was from very small blood vessels presumably capillary in nature. Likewise the myocardium itself became pink without any trace of reduced venous blood.

The following experiment was done. The graft was placed and the sinus was completely occluded. The circumflex ramus of the left coronary artery was ligated and the artery was severed distal to the occlusion. India ink was injected into the graft and within a few moments the ink was identified in the retrograde flow from the severed artery. This does not necessarily indicate that the particles of ink traversed the capillary bed. Direct communications between the venous system without the interposition of the capillary bed are illustrated in *A* and *B* of Fig. 1. Direct communications between the arterial system and the venous system without the interposition of the capillary bed are also illustrated in this specimen.

DIRECT COMMUNICATIONS BETWEEN ARTERIES AND VEINS AND VEINS AND ARTERIES WITHOUT INTERPOSITION OF A CAPILLARY BED

Such communications have been described by Prinzmetal, Simkin, Bergman, and Kruger[11] in the human heart and in the dog heart. These communications were never observed in the specimens of normal dog hearts in this laboratory in which the arteries and veins were injected with a mixture of barium sulfate and gelatin as used by Gross.[12] However, using this same method another collection of specimens in which the two-stage grafting operation had been done shows these communications to be present. It is readily possible to trace on the surface of these cleared specimens communications from the coronary sinus system. The specimen illustrated shows veins filled from arteries and arteries filled from veins. These communications can be seen not to traverse a capillary bed. Also this injection mass is not sufficiently fine to traverse a capillary bed.

CONCLUSION

Evidence is presented which indicates that blood can flow from the aorta, through a graft, into the coronary sinus and its tributaries. From the venous side of the circulation this blood can traverse the capillary bed and emerge from the arterial side of the circulation. In its transit through the capillary bed this blood gives up its oxygen. This retrograde circulation through the capillary bed can explain the benefit that this two-stage operation gives to the heart in the presence of coronary artery occlusion. Some of these specimens showed communications between arteries and veins and between veins and arteries without the interposition of a capillary bed.

REFERENCES

1. Beck, C. S., Stanton, E., Batiuchok, W., and Leiter, E.: Revascularization of the Heart by Graft of Systemic Artery Into Coronary Sinus, J. A. M. A. **137**:436, 1948.
2. Beck, C. S.: Revascularization of the Heart, Ann. Surg. **128**:854, 1948.
3. Beck, C. S.: Revascularization of the Heart, Surgery **26**:82, 1949.
4. McAllister, F. F., Leighninger, D. S., and Beck, C. S.: Revascularization of the Heart by Vein Graft From Aorta to Coronary Sinus, Ann. Surg. **133**:153, 1951.
5. Stanton, E., Schildt, P., and Beck, C. S.: The Effect of Abrasion of the Surface of the Heart Upon Intercoronary Communications, AM. HEART J. **22**:529, 1941.
6. Hahn, R. S., and Beck, C. S.: Revascularization of the Heart. A Study of Mortality and Infarcts Following Multiple Coronary Artery Ligation, Circulation **5**:801, 1952.
7. Leiter, E.: The Electrocardiogram Following Anastomosis of Carotid Artery to Coronary Sinus, AM. HEART J. **30**:125, 1950.
8. Heimbecker, R., Thomas, V., and Blalock, A.: Experimental Reversal of Capillary Blood Flow, Circulation **4**:116, 1951.
9. Gregg, D. E., and Dewald, D.: The Immediate Effects of the Occlusion of the Coronary Veins on the Dynamics of the Coronary Circulation, Am. J. Physiol. **124**:435, 444, 1938.
10. Gregg, D. E., Thornton, J. J., and Mautz, F. R.: The Magnitude, Adequacy and Source of the Collateral Blood Flow and Pressure in Chronically Occluded Coronary Arteries, Am. J. Physiol. **127**:161, 1939.
11. Prinzmetal, M., Simkin, B., Bergman, H. C., and Kruger, H. E.: Studies on the Coronary Circulation. II. The Collateral Circulation of the Normal Human Heart by Coronary Perfusion With Radioactive Erythrocytes and Glass Spheres, AM. HEART J. **33**:420, 1947.
12. Gross, L.: The Blood Supply to the Heart, New York, 1921, Paul B. Hoeber, Inc.

THE INTRAMUSCULAR ADMINISTRATION OF PROCAINE AMIDE

A Safe and Effective Method for the Treatment of Cardiac Arrhythmias

Charles D. Enselberg, M.D., and Martin Lipkin, M.D.*

New York, N. Y.

IN THE treatment of urgent cases of certain cardiac arrhythmias, the intravenous administration of procaine amide has become increasingly popular. However, this mode of administration is not entirely free of danger, as will be discussed below. Therefore, it was decided to study the effects of intramuscular use of the drug and to determine whether the latter method is therapeutically feasible.

METHOD

Six cats and fourteen rabbits received intramuscular injections of 0.25 c.c. of 10 per cent procaine amide hydrochloride (Pronestyl Hydrochloride); the rabbits also received similar quantities of 13 per cent procaine amide levulinate, and 15.9 per cent procaine amide gluconate. Observations were made for evidence of pain, and histologic examination of the injected tissues was carried out at intervals of every two and seven days.†

Blood plasma concentrations of procaine amide were determined in thirteen patients at intervals after the intramuscular injection of the drug. The chemical method consisted of extraction with ether from alkalinized plasma, back extraction with hydrochloric acid, diazotization, and addition of the Bratton and Marshall reagent. The color was read in the spectrophotometer at 540 $\mu\mu$.†

Procaine amide was given intramuscularly to sixty-two patients having a variety of rhythmic mechanisms. A total of eighty-one injections was given, chiefly in the buttocks. The drug was administered undiluted in single doses ranging from 0.1 to 2.5 Gm., the usual dose being 1.0 Gm. (10 c.c. of Pronestyl solution). Some patients received two or three injections at intervals of from one to three hours, and one patient received 1.0 Gm. every three hours for a total of 8.0 Gm. in twenty-four hours.

Control observations were made of the blood pressure and electrocardiogram, and follow-up observations at intervals of from three to fifteen minutes. Patients were questioned as to pain, headache, giddiness, nausea, or other unpleasant symptoms. The injection sites were examined for evidence of local tissue reaction.

From the New York Polyclinic Medical School and Hospital, New York, N. Y.
Received for publication June 25, 1952.

*Resident in Medicine.

†These studies were performed at the laboratories of E. R. Squibb & Sons at New Brunswick, N. J.

RESULTS

Supraventricular Arrhythmias.—In two patients with frequent supraventricular premature systoles single doses of 1.0 Gm. were ineffective. In a third case the premature beats were moderately reduced. In three patients with auricular or nodal tachycardia there was no effect after 1.0 Gm. One case of nodal tachycardia was unaffected by a total of 8.0 Gm. (1.0 Gm. every three hours). In another case of nodal tachycardia normal rhythm appeared fifteen minutes after the injection of 1 Gm., but one minute later the paroxysm recurred.

Four cases of auricular flutter and four cases of chronic auricular fibrillation were unsuccessfully treated with doses of 1.0 to 2.0 Gm. every hour or two up to a total dose of 4.0 to 4.5 Gm. Slowing of the auricular rate occurred in all the cases of flutter, and temporary conversion to flutter developed in three of the cases of fibrillation. Two patients developed "paradoxical tachycardia," the ventricular rate rising as the auricular rate slowed.

Ventricular Arrhythmias.—Two cases of ventricular tachycardia were converted to normal rhythm within fifteen minutes after doses of 0.2 and 1.0 Gm. In eleven out of fourteen cases, frequent ventricular premature systoles including bigeminy were completely abolished after single doses of 0.5 to 1.5 Gm. The onset of effects appeared in three to fifteen minutes; peak action, in fifteen to forty-five minutes; and the effects lasted two to ten hours after a single dose.

Normal Rhythm.—Twenty-nine patients with regular sinus rhythm showed no alteration of rate or rhythm, and no electrocardiographic change beyond occasional prolongation of the QRS complex up to 0.02 second. These patients received a single dose of 1.0 Gm.

Blood Pressure.—Observations were made on forty-nine patients. In twelve there was either no change or a slight rise. In thirteen there was a fall in systolic pressure of less than 10 per cent of control levels. In the remaining twenty-four cases the blood pressure fell 10 per cent or more; the systolic pressure being affected in all these cases, while the diastolic levels were changed less often and to a smaller degree. The greatest decline occurred in a patient fifteen minutes after a 1.0 Gm. dose, when his pressure fell from 250/88 to 168/80 mm. Hg and gradually rose in the next two hours to 190/100 mm. Hg. Six others exhibited declines of 20 to 30 per cent, while the remaining seventeen patients had blood pressure reductions between 10 and 20 per cent. In no instance was the hypotensive effect associated with troublesome symptoms, despite the fact that many patients were not confined to bed. Hypotensive action was noted as early as ten minutes after injection; maximum effects, usually in one hour with a range of fifteen to one hundred twenty minutes; the duration of effect was one to four hours. Repetition of the dose at one- or two-hour intervals caused little or no increase in hypotension.

Blood Levels.—Plasma concentrations of procaine amide are shown in Table I.

TABLE I. BLOOD PLASMA CONCENTRATION OF PROCAINE AMIDE IN MG./L. AFTER INTRAMUSCULAR ADMINISTRATION

CASE	3 MIN.	4 MIN.	5 MIN.	6 MIN.	8 MIN.	1 HR.	4 HR.	6 HR.
1			2.2			13.4	3.0	
2			2.1			5.2	2.6	
3				5.1		4.7	1.7	
4	2.1					(?)-52.4	1.0	
5		2.1				(?)-26.0	1.2	
6			10.6			7.2	6.6	
7					4.8	6.0	3.0	
8			4.8			3.6	3.4	
9			(?)-50.4			5.4	3.9	
10			18.1			3.3		2.5
11			2.6			2.4		2.2
12			4.4			3.4		2.2
13			3.7					

(?) = Possible technical error.

Pain and Local Reaction.—In none of the animals was there any indication of pain following injection of the drug. Pain was not experienced by any of the patients except at the moment of needle puncture.

Local tissue reactions occurred in the animals. Small hemorrhagic areas and very slight muscle degeneration were seen two days after injection. After seven days there was no evidence of muscle degeneration and practically no trace of hemorrhage at the sites of the hydrochloride injections, and slightly more severe reactions at the sites of the levulinate and gluconate injections.

One patient, after five daily injections of 1.0 Gm., complained of a sense of a lump or fullness in the buttock; but no objective evidence was found of any mass or inflammation, and the symptom disappeared overnight. In four cases injection was made into the deep subcutaneous tissues of the deltoid region of the arm, using 0.5 Gm. in each instance. Neither in these patients nor in the remainder of the whole clinical group, who received the drug intragluteally, was there any indication of local tissue irritation such as a mass, swelling, tenderness, or redness.

Untoward Symptoms.—Discomfort attributable to the intramuscular administration of the drug was rare. One patient became dizzy for a few seconds about ten minutes after a 1.0 Gm. dose, but the blood pressure remained unchanged. Two patients complained of moderately severe headache an hour after injection, but the blood pressure was altered in only one of them (190/110 to 170/90 mm. Hg). Another patient experienced dizziness at a time when the blood pressure was higher than the control level. In none of these cases was the symptom severe. The only instance of great discomfort occurred in a patient with auricular fibrillation who received 4.5 Gm. in four hours. As the auricular rate declined, the ventricular rate rose from 100 to 140 per minute, with distressing dyspnea accompanying the tachycardia.

DISCUSSION

Antiarrhythmic Effects.—Our failures in supraventricular arrhythmias were not unexpected in the light of reported experience,[1-4] and lead us to accept the view that procaine amide has preferential action against ventricular arrhythmias. Nevertheless, others have reported clinical and experimental evidence of favorable action in auricular arrhythmias.[5-8] The response of our cases of ventricular arrhythmias was parallel to the general experience with intravenous and oral administration of the drug. Although we had only two cases of ventricular tachycardia, we were gratified by their quick response to intramuscular procaine amide.

Hypotensive Effects.—A fall in blood pressure has been noted in practically all the publications on procaine amide. However, the potential gravity of this action has been stressed only in more recent papers,[3,9] in which it is pointed out that severe hypotension with disturbing symptoms may occur after small doses intravenously, and even with infusion rates as slow as 25 mg. per minute. The mechanism of the hypotension is not entirely clear, but recent studies indicate that the chief cause is probably a direct myocardial depressant action.[10] Following intravenous injection there is a fall in cardiac output accompanied by a decrease in systemic arterial pressure and a diminution in pulmonary blood flow, while changes in peripheral resistance are inconstant. It is scarcely necessary to stress the ominous possibilities of such effects in serious cardiac arrhythmias such as ventricular tachycardia complicating myocardial infarction.

Blood pressure data are often incomplete in the publications on procaine amide, and we ourselves made no direct comparisons of intravenous and intramuscular administration. It is therefore difficult to compare the frequency and severity of hypotensive effects of these routes of administration. However, since we observed no serious reactions in our cases, and since the degree of hypotension associated with intramuscular injection appears to be slight to moderate, we conclude that the hypotensive effects are mitigated by this mode of administration. Alarming and even fatal hypotension has occurred after intravenous injection. It is also possible that some of the reported cases of sudden death after the latter mode of administration[1,3,4,11] may have occurred as a consequence of abrupt increase of drug concentration in the blood stream. Absorption from an intramuscular site may be expected to produce a less rapid increase in concentration, and thereby possibly diminish the danger of ventricular fibrillation and standstill. The published data on procaine amide levels in the blood are scanty. A concentration of 17 mg./L. of plasma has been noted five minutes after 1.0 Gm. of procaine amide intravenously.[12] Higher concentration might occur earlier. In our cases, plasma levels in the first few minutes after intramuscular injection were generally between 2 and 10.6 mg./L.

Pain and Local Reactions.—Procaine amide hydrochloride is available in sterile aqueous solution (Pronestyl Hydrochloride, E. R. Squibb & Sons) containing 1.0 Gm. in 10 c.c., with a pH of 5.6. It is important, therefore, to be certain that no harmful reactions are provoked by the large volumes required or by the acidity of the preparation. So far as pain is concerned, we were im-

pressed by its absence. As for the local tissue irritation found histologically in the injected animals, it was no more severe than that found after intramuscular injection of other therapeutic preparations such as liver extract and several accepted multiple vitamin and B vitamin solutions.[13] The insignificance of the local tissue irritation is borne out by the fact that none of the patients exhibited evidence of local reaction, even though as much as 2.0 Gm. (20 c.c. of solution) was injected into a single site at one time. We feel that the good local tolerance of the drug is probably due to its anesthetic properties as well as to its rapid absorption.

Speed of Action.—Our data indicate that the onset of action after intramuscular injection is generally within fifteen minutes. In responsive arrhythmias it may be as short as three minutes. Peak effects occur well within one hour. Effective action lasts for two to ten hours, depending upon the dose and the responsiveness of the arrhythmia. These characteristics are much closer to those of intravenous than of oral administration, and justify our belief that the intramuscular route can serve as a substitute for intravenous injection.

Recommendations for Therapeutic Use.—There is no doubt that the safest method of giving procaine amide is by mouth. Nevertheless there are distinct indications for parenteral administration: when the patient is unable to swallow or retain the oral preparation, and in cases where the clinical condition is urgent. In these circumstances the intramuscular route should be preferred to the intravenous for the following reasons:

1. A smaller likelihood of producing serious hypotension or grave arrhythmias associated with the possibility of sudden death.
2. Sufficiently rapid onset of effective action.
3. Absence of pain and local tissue reaction.

An initial dose of 1.0 Gm. should be adequate for most conditions, subsequent doses depending upon response. For ventricular premature systoles subsequent doses of 0.5 to 1.0 Gm. at intervals of two to six hours are recommended. For ventricular tachycardia a dose of 1.0 to 2.0 Gm. followed by 1.0 Gm. every one to three hours is recommended. Auricular arrhythmias may require even larger doses.

SUMMARY AND CONCLUSIONS

1. Procaine amide (Pronestyl) hydrochloride was given intramuscularly to sixty-two patients with various rhythmic mechanisms, in single doses of 0.1 to 2.5 Gm., and total doses of 0.2 to 8.0 Gm.

2. In this series preferential action was shown against ventricular arrhythmias. Two cases of ventricular tachycardia were successfully treated.

3. Mild to moderate hypotension occurred in one-half the cases; serious hypotension in none.

4. The onset of drug action appeared three to fifteen minutes after injection, peak effects well within one hour, and dissipation of effects two to ten hours after a single dose.

5. The intramuscular route is painless, and despite the large volumes required and the acidity of the solution it causes no significant local tissue reaction.

6. Recommended doses are 0.5 to 2.0 Gm. initially, and 0.5 to 1.0 Gm. later at intervals of one to six hours depending upon the severity and response of the arrhythmia.

7. It is concluded that intramuscular injection is preferable to intravenous as a parenteral method because it is safer and because it yields sufficiently rapid results in most cases.

The authors are most grateful to Dr. Arthur C. De Graff for his valuable suggestions in the course of this study. We wish to thank the following physicians for permitting us to include their patients: Drs. James P. Croce, Sr., Emanuel Hellman, Grover J. Sprague, and Robert Wallach.

REFERENCES

1. Kayden, H. J., Steele, J. M., Mark, L. C., and Brodie, B. B.: The Use of Procaine Amide in Cardiac Arrhythmias, Circulation **4**:13, 1951.
2. Miller, H., Nathanson, M. H., and Griffith, G. C.: The Action of Procaine Amide in Cardiac Arrhythmias, J.A.M.A. **146**:1004, 1951.
3. Berry, K., Garlett, E. L., Bellet, S., and Gefter, W. I.: Use of Pronestyl in the Treatment of Ectopic Rhythms. Treatment of 98 Episodes in 78 Patients, Am. J. Med. **11**:431, 1951.
4. Kinsman, J. M., Hansen, W. R., and McClendon, R. L.: Procaine Amide (Pronestyl) in the Treatment of Cardiac Arrhythmias. Am. J. M. Sc. **222**:365, 1951.
5. Schaffer, A. I., Blumenfeld, S., Pitman, E. R., and Dix, J. H.: Procaine Amide: Its Effects on Auricular Arrhythmias, Am. Heart J. **42**:115, 1951.
6. Schlachman, M., Benjamin, J. W., and Terranova, R.: The Termination of Auricular Fibrillation in Dogs With Procaine Amide Hydrochloride, Am. Heart J. **42**:284, 1951.
7. Schaffer, A. I.: Procaine Amide Compared With Quinidine as a Therapy for Arrhythmias, Am. Heart J. **42**:597, 1951.
8. McCord, M. C., and Taguchi, J. T.: A Study of the Effect of Procaine Amide Hydrochloride in Supraventricular Arrhythmias, Circulation **4**:387, 1951.
9. Stearns, N. S., Callahan, E. J., III, and Ellis, L. B.: Value and Hazards of Intravenous Procaine Amide ("Pronestyl") Therapy, J.A.M.A. **148**:360, 1952.
10. McClendon, R. L., Hansen, W. R., and Kinsman, J. M.: Hemodynamic Changes Following Procaine Amide Administered Intravenously, Am. J. M. Sc. **222**:375, 1951.
11. Wedd, A. M., Blair, H. A., and Warner, R. S.: The Action of Procaine Amide on the Heart, Am. Heart J. **42**:399, 1951.
12. Mark, L. C., Kayden, H. J., Steele, J. M., Cooper, J. R., Berlin, I., Rovenstine, E. A., and Brodie, B.: The Physiological Disposition and Cardiac Effects of Procaine Amide, J. Pharmacol. & Exper. Therap. **102**:5, 1951.
13. Console, A. D.: Personal communication, based on work done at E. R. Squibb & Sons laboratories by Drs. B. G. H. Thomas and C. E. Linegar.

CLINICAL STUDIES OF INTRAMUSCULAR INJECTION OF DIGITOXIN (DIGITALINE NATIVELLE)* IN A NEW SOLVENT

VICTOR STRAUSS, M.D., DAVID L. SIMON, M.D., ARNOLD IGLAUER, M.D., AND JOHNSON MCGUIRE, M.D.

CINCINNATI, OHIO

A THERAPEUTIC effect can usually be produced by the oral administration of digitalis preparations.[1] However, parenteral administration of digitalis glycosides may be administered to patients with congestive failure or with arrhythmias who are comatose, nauseated, or uncooperative or whose surgical condition might preclude the use of the oral form.

The intravenous route should be reserved for cardiac emergencies when speed is of the essence and minutes rather than hours are important.[1,2] Under such circumstances ouabain may be used. In other cases a parenteral form of equal efficacy with the oral is desirable. Digitalis glycosides in alcoholic solution, intended primarily for intravenous administration, have been given intramuscularly on occasion, but usually produce severe pain locally, and may produce tissue necrosis, and have not been consistent in their effect because of the irregularity of their absorption.[2-4] To overcome these hazards it was necessary to find a new solvent that would be nontoxic and nonirritating when injected intramuscularly. The combination of polyethylene glycol 300 39 per cent, benzyl alcohol 4 per cent, ethyl alcohol 4 per cent, distilled water 19 per cent, and glycerine 44 per cent has been found to have these properties.[4,5,6]

METHOD

Digitoxin (Digitaline Nativelle) was dissolved in the above preparation, and the solution was evaluated in twenty-one patients with auricular fibrillation and congestive heart failure. Only patients with auricular fibrillation were chosen because it was felt that the therapeutic effect of digitoxin could be most adequately evaluated in them, and that observation of the ventricular rate and T-wave change, electrocardiographically, furnished valid criteria of the degree of digitalization.

From the Cardiac Laboratory, Cincinnati General Hospital and the Department of Internal Medicine, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

This paper was read by title at the 25th Scientific Session of the American Heart Association, Cleveland, Ohio, April 18, 1952.

This paper will be read at the Regional Meeting of the American College of Physicians Nov. 22, 1952, at Chicago, Ill.

Received for publication July 28, 1952.

*The material for this study was furnished by the Varick Pharmacal Co., Inc., New York, N. Y.

Digitalis preparations were withheld in patients who had auricular fibrillation until the ventricular rate became rapid, with a pulse deficit, and signs and symptoms of cardiac failure appeared. An electrocardiogram was then taken, and digitalization was initiated by an intramuscular injection of 0.6 mg. (3 c.c.) of digitoxin in each gluteus maximus, a total of 1.2 mg. Later, for purposes of comparison, digitoxin (Digitaline Nativelle) was administered orally in identical dosage in eleven patients. Eight of these patients had been previously treated by the intramuscular route.

The onset of ventricular slowing and the appearance of digitalis changes were determined by electrocardiograms taken at hourly intervals for four hours following injection. Twenty-one patients were maintained on an average daily dosage of 0.2 mg. for up to twenty-eight days, the average maintenance period being nineteen days. At the conclusion of the study of parenteral administration the patients were transferred immediately to the oral form without change in the dosage.

MATERIAL

A random selection of patients with auricular fibrillation in failure was made from the Cardiac Clinic of the Cincinnati General Hospital. There were fifteen men and six women. Sixteen were white and nine were Negroes. The youngest was 37 and the oldest was 75 years of age. The diagnoses varied as follows: hypertensive or coronary artery disease, twelve; rheumatic heart disease, six; syphilitic heart disease, two; and post-partum myocarditis, one.

RESULTS

Decrease of the initial ventricular rate occurred following rapid intramuscular digitalization in all patients (Fig. 1; Table I). The average initial ventricular rate was 100 per minute (range 120 to 60 per minute). At the end of four hours after the intramuscular injection of digitoxin, the average ventricular rate was 77 per minute (range 110 to 50 per minute). Further fall in rate twenty-four hours later was noted in patients in whom the rate remained relatively rapid at the end of four hours. Ventricular rate could be kept at the desired level (65 to 85 per minute) by intramuscular maintenance dosage (0.2 mg.) in all of the patients so treated. Signs and symptoms of congestive heart failure were controlled in all patients. In some the clinical status seemed to be improved in comparison with previous periods of oral therapy.

Very slight to moderate pain followed the injection of the initial digitalizing dose, but it was never severe enough to interfere with muscle function. The maintenance dose usually did not produce pain. No abscess or nodule formation was noted at any time, and there were no toxic or allergic reactions to the solvent. At the termination of the study the patients were transferred to the oral form on dosages equal to that of the intramuscular and they maintained the established ventricular rate.

The procedure described above, but using the oral form, was repeated on eleven patients (eight of whom had previously been on the intramuscular form).

The average initial pulse rate in the intramuscular group was lower than in the oral group because at the time of the study, due to the condition of the patients in the intramuscular group, we felt it incumbent upon us to institute the parenteral therapy in this group before the higher rates obtained in the oral group occurred. In all other respects—speed of digitalis effect, final pulse rate, ease of maintenance—the studies were comparable (Fig. 1; Table I).

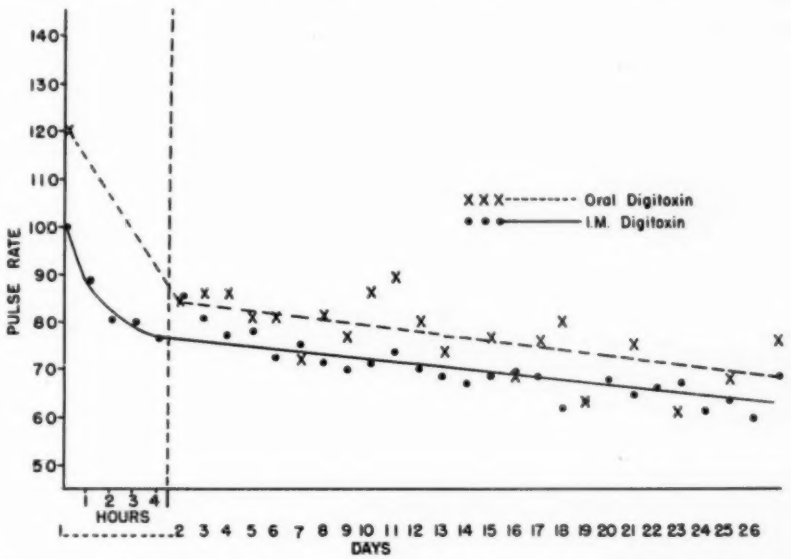


Fig. 1.—Chart showing comparable results obtained with oral and intramuscular digitoxin. Curves represent pulse rates plotted against time with oral and intramuscular digitoxin.

DISCUSSION

The solution of digitoxin used in this study produced prompt and satisfactory digitalis effects. Gold[2] has shown that oral or intravenous administration of a single digitalizing dose of digitoxin produced a fall in ventricular rate in patients with auricular fibrillation which is marked within four or five hours. The curve obtained by plotting average ventricular rate in our observations is very similar to those depicted in his articles. Slowing of ventricular rate has long been accepted as a criterion of digitalis effect; in the present observations, adequate control of signs and symptoms of congestive failure was also produced by intramuscular administration of digitoxin. Mild local irritation occurred in some patients following injection of 1.2 mg. of digitoxin, but this was not severe enough to contraindicate its use. In fact, it seemed about equal to the local discomfort produced by many other drugs in common use, such as liver extract and vitamin B preparations. While it is appreciated that the ideal maintenance doses varies in different patients, for the purposes of this study 0.2 mg. daily was employed. Maintenance dosages usually produced no discomfort or induration at the site of injection.

Toxicity.—The principal ingredient of the solvent is polyethylene glycol 300. Compounds of this class, commercially known as Carbowax, have been the

TABLE I.

PATIENT	AGE (YRS.)	COLOR	SEX	PAIN		DIAGNOSIS*	BEFORE DIGITALIS	HOURS				FIRST DAY	LAST DAY
				INITIAL	MAINTENANCE			1	2	3	4		
Intramuscular													
1. R. D.	60	N	F	+	0 → +	RHD	115	115	100	95	90	80	60
2. G. H.	70	N	M	++	0 → +	H & ASCVD	90	90	80	75	78	72	60
3. S. B.	49	N	M	+	0	SYPH. H.D.	108	90		85	80	88	70
4. P. J.	74	W	M	0	0 → Tr.	H & ASCVD	115	100	90	85	90	88	68
5. G. L.	65	N	M	++++	0 → +	H & ASCVD	90	85	85		85	85	60
6. H. A.	43	W	F	+++	0 → ++	RHD	90	85	80	70	65	88	80
7. C. W.	72	W	M	++	0 → ++	HCVD	60	60	50		50	76	60
8. H. B.	57	N	F	++	0 → ++	HCVD	100	90	80		50	80	68
9. J. D.	45	W	M	+	0 → ++	HCVD	95	90	85	85	90	88	68
10. F. J.	69	W	F	++++		RHD ASHD	90	90		86	82	72	72
11. W. T.	70	N	M	+	0 → ++	ASHD	105	95	70		70	92	68
12. R. B.	45	N	M	++	0 → +	RHD	95	85	80	75	75	76	60
13. O. S.	56	N	M	+	0 → +	SYPH. H.D.	85	72	60	75		88	60
14. A. I.	75	W	M	0	0	HCVD	95	85	78	75	75	68	60
15. E. A.	71	W	M	++	0 → +	HCVD	105	88	85	80	78	80	64
16. W. S.	72	W	M	0	0 → +	H & ASCVD	88	82	75	88	90	84	76
17. S. F.	65	W	M	++++	0 → +	RHD	100	64	60	58	58	80	64
18. H. J.	72	W	M	+	0 → +	H & ASCVD	120	110	105	95	110	108	68
19. C. R.	68	W	M	++	0	H & ASCVD	120	110	90	90	90	88	88
20. B. P.	42	W	F	++	++	RHD	105	100	100		80	76	80
21. O. M.	37	N	F	0	0 → +	P.P. MYOCARD	120	85	75	75		100	76
							Σ = 2091	1871	1613	1201	1234	1877	1430
							n = 21	21	20	15	16	22	21
							x = 100	89	81	80	77	85	68

Oral													
1.	A. S.	74	W	M			H & ASCVD	140	130	115	110	90	64	64
2.	R. D.	60	N	F			RHD	140					92	64
3.	G. H.	70	N	M			H & ASCVD	116					76	64
4.	P. J.	74	W	M			H & ASCVD	128					84	72
5.	G. L.	65	N	M			H & ASCVD	112					84	60
6.	H. B.	57	N	F			HCVD	112					84	76
7.	J. D.	45	W	M			HCVD	120					88	88
8.	A. I.	75	W	M			HCVD	100					84	64
9.	A. F.	49	W	F			RHD	132					96	76
10.	R. B.	45	N	M			RHD	112					92	84
11.	A. S.	47	N	M			RHD	120					80	64
								$\Sigma =$ 1332	130	115	110	90	924	776
								$n =$ 11	1	1	1	1	11	11
								$\bar{x} =$ 121	130	115	110	90	84	71

*Key:

RHD = Rheumatic heart disease.
Syph. H.D. = Syphilitic heart disease.
HCVD = Hypertensive cardiovascular disease.
ASHD = Arteriosclerotic heart disease.
P.P. Myocard. = Post-partum myocarditis.
Tr. = Trace.

subject of pharmacologic and toxicologic study for ten years. They have been employed extensively in preparations for external application, but use of them for injection is relatively recent. In animals, intraperitoneal and intravenous dosage of a magnitude sufficient to produce maximal digitalis effect have caused no toxic changes in the liver or kidney. Intramuscular injection of 2 Gm./kg. in dogs and rats produced local necrosis change in muscles, but again this range of dosage is much greater than that employed in the present study. Accidental intravenous injection need not be feared since the $L.D._{50}$ for this material by intravenous route is 7.1 ml./kg. in rats, yet the maximal amount that need be given an average sized man in a single injection is 0.4 ml./kg. In both man and animals, it has been shown that polyethylene glycols are promptly excreted by the kidney, nearly all being recoverable in the urine within forty-eight hours after injection. Evidence indicates that these compounds are excreted by the renal glomeruli without reabsorption by the tubules. Even in the presence of renal disease or congestive heart failure, glomerular filtration rate would undoubtedly remain high enough so that polyethylene glycol would not accumulate within the body.[4,5,6]

Benzyl alcohol is also present in the solvent in concentration of 4 per cent. Use of this material for local anesthesia in concentrations of 1 to 4 per cent is sanctioned by the *Council of Pharmacy and Chemistry of the American Medical Association*, and it has been listed in *New and Nonofficial Remedies* for many years. Ethyl alcohol in 4 per cent concentration is too dilute to produce local tissue necrosis manifested by high concentrations of this material. Glycerine has been used as a solvent in injectable preparations for many years without untoward local or systemic reaction.

CONCLUSION

1. Digitoxin in a new solvent for intramuscular use was studied in twenty-one patients and found to be safe and effective in initiation and maintenance of digitalization.

2. A satisfactory therapeutic effect was obtained with minimal local and no undesirable systemic effects.

3. Further trials of digitoxin in this solvent are suggested with patients requiring parenteral therapy.

Subsequent to the admission of this manuscript for publication, Gold et al., in Am. J. Med. **8**:2, 1952, showed that Digoxin, lanatoside C, digitoxin, and Digifolin, administered parenterally, produced thereapeutic effects with marked reduction in nauseating and emetic effects when compared with the oral administration of the same drugs.

REFERENCES

1. Goodman, Louis, and Gilman, Alfred: The Pharmacological Basis of Therapeutics, New York, 1941, The Macmillan Company.
2. Gold, Harry: The Choice of a Digitalin Preparation, Connecticut M. J. **9**:193, 1945.
3. Gold, Harry: The Treatment of Cardiac Failure With Digitalis Glycosides, Mod. Concepts Cardiovas. Dis. **14**:11, 1945.
4. Smyth, Henry F., Jr., Carpenter, Charles P., and Weil, Carrol S.: The Toxicology of the Polyethylene Glycols, J. Am. Pharm. A., Sci. Ed. **39**:349, 1950.
5. Shaffer, C. Boyd, Critchfield, Frances H., and Nair, John H., III: The Absorption and Excretion of a Liquefied Polyethylene Glycol, J. Am. Pharm. A., Sci. Ed. **39**:340, 1950.
6. Mellon Institute of Industrial Research, Univ. of Pittsburgh: Special Report on Parenteral Administration of Polyethylene Glycol 300 W and 400 W, Confidential Report, July 12, 1950.

Clinical Reports

ACQUIRED ARTERIOVENOUS FISTULA

A Case of Over Twenty Years' Duration Operated Upon

George A. Pipilis, M.D., and B. Stavrakas, M.D.

Athens, Greece

THE ACQUIRED arteriovenous fistula, or arteriovenous aneurysm, usually is the sequella of trauma by gunshot or stab wounds resulting in a direct communication between an artery and a vein.[1] The direct shunt of the blood from an artery to a vein causes disturbances of the general circulation and imposes a strain on the heart.

The circulatory disturbances may be severe, such as cardiac failure and ulceration or rupture of the proximal end of the fistula or artery.

The present case represents an arteriovenous fistula of a small branch of the axillar artery, of twenty years' duration, accompanied by cardiac insufficiency of Class II functional capacity.

CASE REPORT

B.K., a 44-year-old white married man, was examined for the first time by one of us in February, 1951. He complained of dyspnea on exertion, easy fatigue, palpitations, and buzzing sensation of the chest and the head. The patient was wounded in 1932 by gunshot at the right subclavian area with exit of the bullet in the posterior axillar area. He recalled that he lost a great amount of blood, and that the trauma healed uneventfully. Several months after the wound, the patient felt by palpation a thrill in the right axilla. Two years later he became dyspneic on exertion and he complained of palpitations. In 1940 he felt in his right axilla a pulsating mass which gradually increased in size with a thrill.

During the last three years the dyspnea on exertion increased and his right arm became numb; slight cyanosis and edema appeared after continuous manual work. The patient also felt a "buzz" on the right chest, especially during the night, reflecting to the mouth and the head.

The physical examination revealed a well-developed man, who did not appear acutely ill. The cardiac limits were slightly enlarged. A faint systolic murmur was heard all over the precordium, more intense at the fourth left intercostal space near the sternum. The lungs were clear. The liver was not enlarged. The right arm seemed slightly edematous, in comparison to the left, and on the upper part there were small new superficial accessory veins. In the right axilla there was palpated a soft pulsating mass approximately the size of a hen's egg. There was a very loud machinery-like continuous bruit and thrill audible all over the right chest. It was impossible to

From the Second Surgical Service of the Evangelismos Hospital, Dr. A. Manos, Director, Athens, Greece.

Received for publication June 26, 1952.

elicit the Branham's sign. The radial pulse was unequal in the two forearms. The blood pressure on the right arm was 105/55 mm. Hg, and on the left 108/70 mm. Hg. The oscillometric reading on the right arm was 1 to 5.5 divisions and on the left 1 to 4. The red blood cell count was 4,800,000; the hemoglobin 14.8 Gm., and the white blood cell count 8,800.

Teleradiography revealed enlargement of the heart with prominent conus (Fig. 1). The electrocardiographic findings (Fig. 3,*A*) were consistent with intraventricular block, unusual electrical position of the heart, and myocardial anoxemia.

The clinical impression was arteriovenous aneurysm of the axillar vessels.

The patient was admitted to the hospital in June, 1951. The laboratory findings (urinalysis, blood urea, blood count, and hemoglobin) were within normal limits. A new electrocardiogram was similar to the previous one. Two older electrocardiograms of the standard leads only, taken in 1940 and 1945, were exactly of the same configuration as the recent ones.

The patient was operated upon June 1, 1951. The aneurysmal sac was excised and the communicating vessels were ligated. The arteriovenous fistula involved the scapular artery (a branch of the axillar artery) and the axillar veins. After the ligation, immediately on the operating table, the bruit disappeared. The postoperative course was uneventful and the patient was relieved of the annoying buzz.

Ten days after the operation the new electrocardiogram (Fig. 3, *B*) disclosed slight change since the previous one. The T waves now became upright in V_5 to V_7, less inverted in V_2 to V_4, and negative in aV_R. The blood pressure was found equal on both arms, 130/85 mm. Hg. The oscillometric reading was also equal on both arms. Teleradiography disclosed a definite reduction shadow (Fig. 2).

On a subsequent follow-up of the patient six months later, the cardiac shadow in roentgenograms was smaller and the electrocardiographic findings were similar to previous ones. The patient complained of some spells of extrasystoles and of dyspnea on exertion to lesser degree than before.

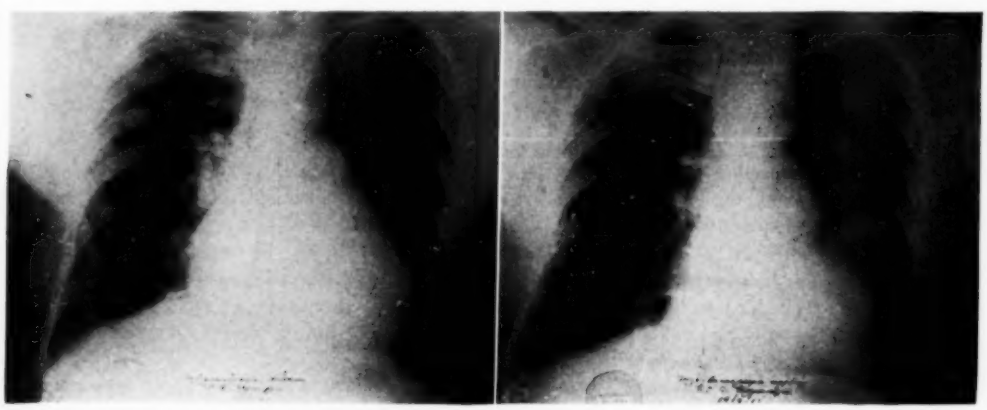


Fig. 1. Fig. 2.

Fig. 1.—Roentgenogram before the operation.
Fig. 2.—Roentgenogram fourteen days after the operation.

DISCUSSION

The present case is an arteriovenous fistula of a small artery, which was well tolerated for a period of twenty years. The most striking findings were the signs of cardiac insufficiency. The cardiac enlargement was not pronounced, because of the small shunt of the blood through the fistula. In cases of arteriovenous fistulas the enhanced stroke output and the accelerated heart rate in-

crease the cardiac output.[2] The larger the arterial shunt the greater is the cardiac enlargement. The cardiac enlargement concerns both ventricles, but the strain of the right ventricle is predominant. The basis of the cardiac enlargement is probably to a great extent dilatation rather than hypertrophy of the ventricle, as evidenced by the rapid reduction of its size after the operation.

Lillehei and associates[3] found in experimental atrioventricular fistulas in dogs that 75 per cent of the cases developed bacterial endocarditis and sometimes endarteritis at the place of the fistula. The excision of infected arteriovenous fistula is reported in the literature.[4] The presence of cardiac failure or the electrocardiographic abnormalities are not contraindications for the operation. The closure of the fistula removes the most serious factor of the overloading of the heart.

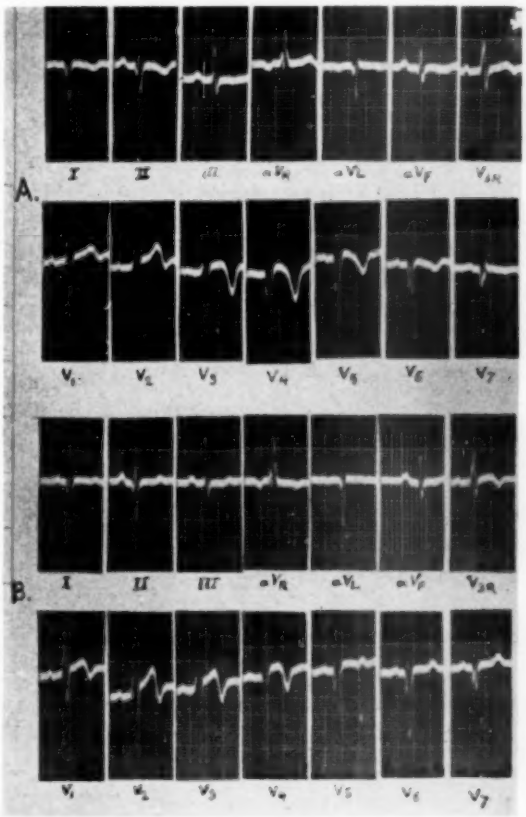


Fig. 3.—Electrocardiograms: *A*. Before the operation. *B*. Ten days after the operation.

The local signs of the arteriovenous communication are the aneurysmal sac, pulsation, and arteriolization of the veins. Because of the shunt of blood from the artery to the vein, a continuous machinery-like bruit with systolic accentuation develops promptly. The Branham's sign is very characteristic in cases of atrioventricular fistulas; when the fistula is closed by digital pressure, the pulse rate decreases. In our case it was impossible to press the fistula located deep under the scapula.

The diagnosis of traumatic arteriovenous fistulas is not a difficult problem. In difficult cases the arteriography helps in exactly locating the fistula. An interval of three to six months is necessary between the development of the fistula and the operation so that a sufficient collateral circulation develops which is capable of preventing ischemia of the limb. The operation is indicated to prevent cardiac damage and cardiac failure.

SUMMARY

A twenty years' duration arteriovenous fistula of the scapular artery in a 44-year-old man has been reported.

The surgical excision of the aneurysmal sac and the ligation of the feeding artery were done.

The permanent cardiac damage was proved by the irreversible electrocardiographic findings six months after the operation.

The cardiac damage and the anoxemia of the myocardium are not contraindications to the operation.

REFERENCES

1. Allen, E. V., Barker, N. W., and Hines, E. A.: Peripheral Vascular Diseases, Chapter XXI, Philadelphia, 1947, W. B. Saunders Company.
2. Friedberg, C. K.: Diseases of the Heart, Philadelphia, 1950, W. B. Saunders Company.
3. Lillehei, C. W., Robb, J. R. R., and Visscher, M. B.: The Occurrence of Endocarditis With Valvular Deformities in Dogs With Arteriovenous Fistulas, Ann. Surg. **132**:577, 1950.
4. Hudson, C. L., and Murray, J. B.: Eberthella Typhosa Infection of Arteriovenous Aneurysm Cured by Excision, J.A.M.A. **141**:130, 1949.

LEAD MYOCARDITIS: REPORT OF A CASE

JOHN L. READ, M.D., AND JOHN P. WILLIAMS, M.D.

RICHMOND, VA.

A REVIEW of the medical literature since 1916 reveals no mention of myocarditis due to lead or of significant electrocardiographic alterations occurring in a patient with lead poisoning. Numerous papers have appeared describing saturnine nephritis, diffuse vascular sclerosis, and arterial hypertension as manifestations of this disease; however, with the exception of Haubrich,[1] no report was encountered which described involvement of the myocardium per se. Haubrich described a 26-year-old woman athlete with an entirely negative previous medical history who was found to have an aneurysm of the heart wall, actually the left auricle, four years after an episode of what was termed lead poisoning. The diagnosis was made on the basis of severe abdominal cramps, diarrhea, dehydration, and malaise which followed the ingestion of apple sauce heated in a pot previously used to melt lead and lined with a residual coating of that metal. Neither blood nor urine determinations of lead were reported. The initial interpretation following fluoroscopy was latent mitral stenosis; however, on the basis of a normal cardiac silhouette four years previously, along with the patient's previous athletic prowess, and the absence of murmurs, this diagnosis was felt to be clinically untenable. In view of the knowledge that lead has been reported to cause primary disturbance of blood supply, it was assumed that secondary parenchymatous degeneration of the myocardium had resulted at the time of her initial dehydration, and an abnormal three-lead electrocardiogram was accepted as substantiating a diagnosis of aneurysm of the left auricle due to lead intoxication. No mention was made of a follow-up on the patient.

In a paper which reviewed this article, Beintker[2] stated that the diagnosis of lead poisoning had not been substantiated because no specific analyses of blood and urine had been presented, no lead line was present, and the objective hematologic and neurological findings usually associated with lead poisoning were not recorded. He felt that it was much more probable that this episode represented an intercurrent and unrelated acute gastrointestinal upset.

ANGINA PECTORIS SATURNINA

The occurrence of symptoms identical to those of angina pectoris has been reported in conjunction with the usual symptom complex induced by lead poison-

From the Cardiovascular Section, Medical Service, McGuire Veterans Administration Hospital, Richmond, Va.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Received for publication July 3, 1952.

ing. In 1926, Hirschfeld[3] reviewed the literature and reported on four additional cases of angina pectoris saturnina. These occurred in young men between the ages of 20 and 28. The attacks were of brief duration and all recovered without subsequent symptoms of angina pectoris. Usually the attacks were abruptly terminated by an eructation or by the passage of flatus. Electrocardiograms were not obtained. The anginal symptoms were believed to result from a spastic action of the poison on the coronary vessels. The author refers to the papers of Stoll[4] and Andral[5] who introduced the term angina pectoris saturnina although similar symptoms accompanying plumbism have been described since antiquity. All cases were reported as having slow pulse rates.

In view of the fact that an extensive review of the literature has failed to reveal an authenticated case of lead poisoning with objective evidence of reversible myocardial damage directly related to lead, it would appear to be worth while to record the following case.

CASE REPORT

J. S., a 39-year-old Negro man, was admitted to the Surgical Service on Jan. 12, 1951, with a tentative diagnosis of acute appendicitis. He complained of severe generalized abdominal cramps of seventy-two hours' duration. These symptoms had become progressively worse and, during the twenty-four hours preceding admission, were associated with nausea, vomiting, anorexia, and the passage of one tarry stool. He also complained of moderately severe, dull, aching pain in the midsternal region, marked weakness, fatigability, and general malaise. The patient was seen by a medical consultant who, on closer questioning, learned that his employment for the past ten weeks had consisted of burning lead storage batteries. He had worn no mask or other form of protection. The system review was not contributory.

Physical Examination on Admission.—The general appearance was that of a fairly well-developed, well-nourished Negro man, who appeared quite pale and who complained of severe abdominal and substernal pain. Examination of the eyes, ears, and nose was normal. Examination of the mouth revealed poor oral hygiene, advanced dental caries, and a distinct lead line. The lungs were clear to auscultation and normally resonant to percussion. The heart was of approximately normal size and configuration. The rate was 48 and regular. Blood pressure was not recorded. There were no murmurs or thrills. Peripheral pulsations were adequate and there was no evidence of edema or venous engorgement. Examination of the abdomen revealed it to be flat to inspection. Palpation revealed generalized tenderness which was particularly severe in the right lower quadrant. There was slight generalized rigidity but no rebound tenderness. The genitalia were normally developed. Rectal examination was normal except for the presence of tarry fecal material. The skin revealed marked pallor. Neurological examination was normal.

Laboratory data at the time of admission revealed red blood cells of 3.2 million with 8.7 Gm. of hemoglobin, white blood cells 9,800 with an essentially normal differential. There was marked basophilic stippling of the red cells and 3 normoblasts per 100 white cells. Sickle-cell preparations were negative. Urinalysis revealed a specific gravity of 1.027. It was negative for sugar, albumin, and formed elements. Serologic test for syphilis was negative. Serum amylase was 59 units (normal 0-60 units); serum sodium 142 meq. per liter; serum potassium 5.3 meq. per liter. Blood chlorides were 598 mg. per cent; serum calcium 9.6 mg. per cent; inorganic phosphorus 2.9 mg. per cent; alkaline phosphatase 3.7 mg. per cent; and acid phosphatase 0.2 mg. per cent. Total proteins were 5.9 Gm. with albumin 3.7 Gm. and globulin 2.2 Gm. A 24-hour urine specimen (2,050 c.c.) contained 0.525 mg. of lead (0.100 mg. per 24 hours' upper limit of normal). The chest roentgenogram was normal. The initial electrocardiogram (Fig. 1) on Jan. 13, 1951, revealed marked sinus depression with multiple ventricular escape beats from varying foci. The S-T segments were coved with inverted T waves in the left precordial leads. The rate was 50.

Clinical Course.—Therapy was initiated promptly and consisted of 3 Gm. of sodium citrate every eight hours with 1 Gm. of calcium lactate four times a day. This regimen was followed for the first five days, at the end of which time he became asymptomatic. The abdominal cramps were relieved by intravenous injection of calcium gluconate. An electrocardiogram (Fig. 2) taken on the third hospital day remained essentially unchanged. From Jan. 17, 1951, until the time of his discharge, his treatment was supplemented by 1 Gm. of sodium phosphate solution four times a day. His hemoglobin was elevated to 14.1 Gm. at the time of discharge, following

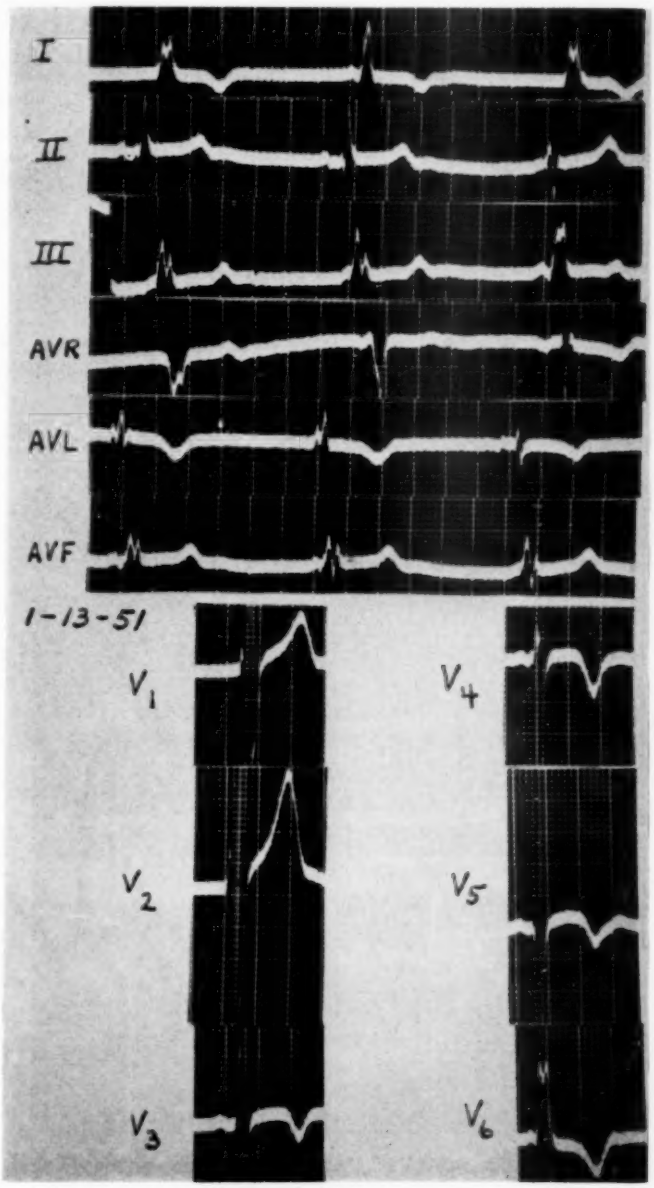


Fig. 1.—Electrocardiogram on Jan. 13, 1951, interpreted as marked sinus depression with multiple ventricular escape beats from varying foci. The S-T segments are coved with inverted T waves in the left precordial leads. The rate is 50.

three 500 c.c. whole blood transfusions. Electrocardiograms (Fig. 3) on Jan. 18, 1951, and thereafter were normal. Serial lead determinations are listed in Table I.

TABLE I

DATE COMPUTED	URINE VOLUME (C.C.)	LEAD CONTENT PER DAY (MG.)
Admission	2,050	0.525
1/18/51	2,300	0.380
1/19/51	1,900	0.505
1/20/52	2,600	0.495
1/21/51	2,500	0.450
1/22/51	2,100	0.385
1/24/51	1,800	0.315
1/27/51	1,850	0.330
1/29/51	1,200	0.200

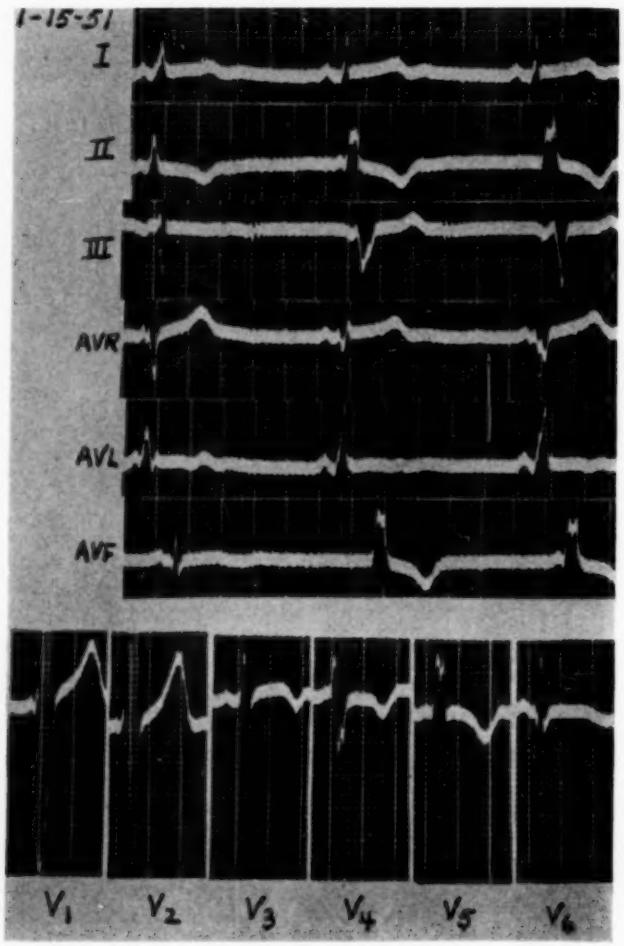


Fig. 2.—Electrocardiogram on Jan. 15, 1951, again interpreted as marked sinus depression with multiple ventricular escape beats from varying foci. The S-T segments are coved with inverted T waves in the left precordial leads. The rate is 50.

The patient was discharged in good health on Feb. 9, 1951. An electrocardiogram (Fig. 4) at this time was essentially normal.

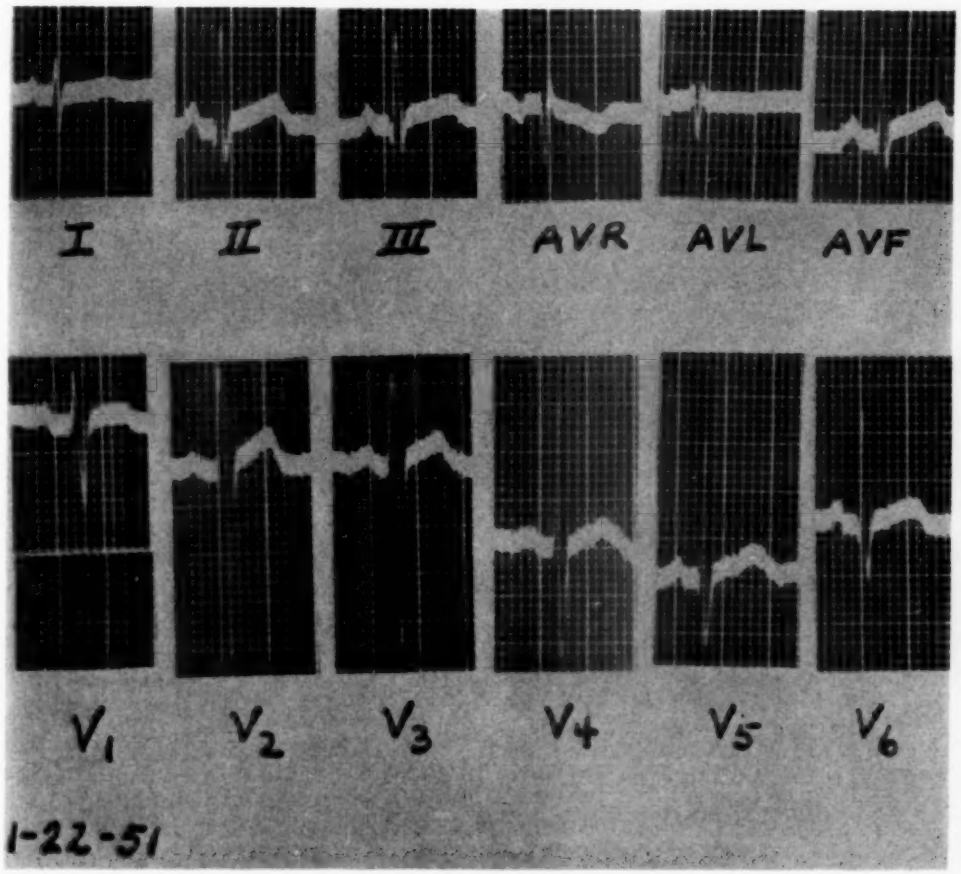


Fig. 3.—Electrocardiogram on Jan. 22, 1951, reveals normal sinus rhythm with a rate of 76. Tracing essentially normal except for low T waves.

DISCUSSION

The absence of histologic studies of the myocardium makes the diagnosis of lead myocarditis a presumptive one. However, the marked depression of the conduction system and T-wave abnormalities in this case with the gradual return of a normal electrocardiogram, paralleling his clinical improvement, suggests a toxic depression of the conduction tissue with toxic changes in the myocardium as the result of lead poisoning. The absence of other diseases and noxious agents, along with normal electrolyte and chemical studies, would tend to eliminate other etiological agents and metabolic factors. The substernal pain and oppression conform with the previous description of angina pectoris saturnina. It is interesting to note that in two subsequent patients with lead poisoning electrocardiograms revealed a bradycardia of 48 and 52. These cases did not however show other abnormalities.

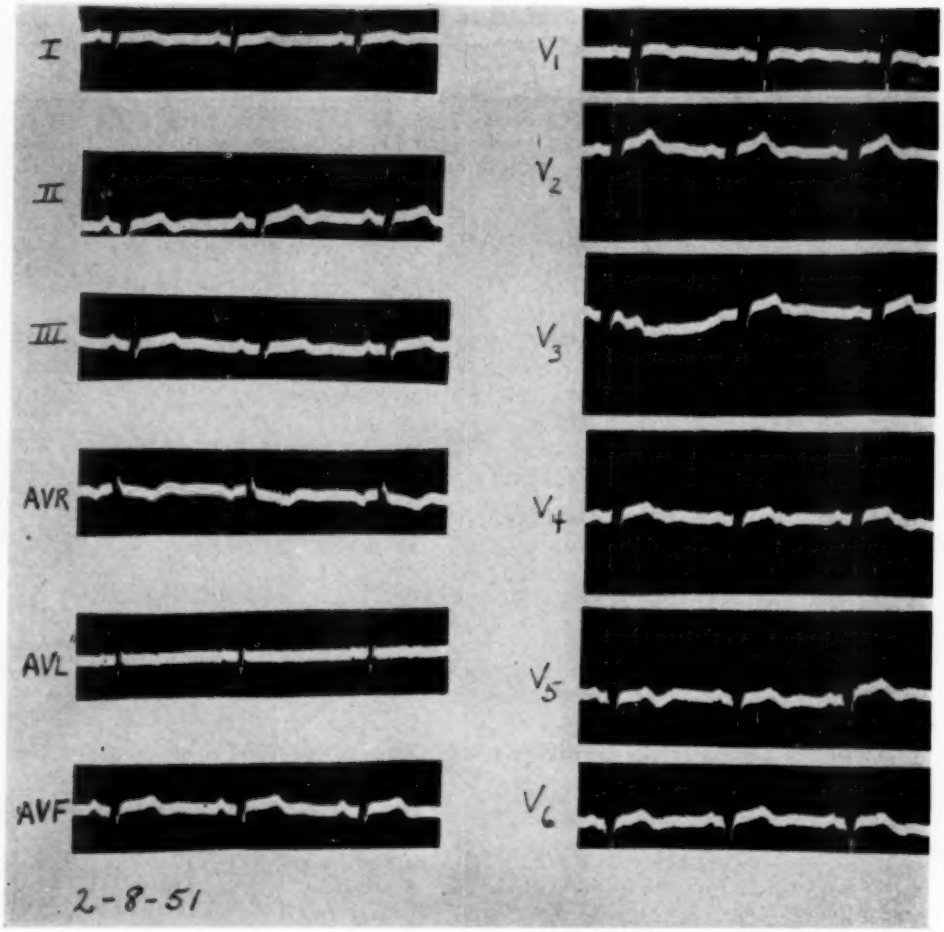


Fig. 4.—Electrocardiogram on Feb. 8, 1951, is essentially normal.

SUMMARY

A case of lead myocarditis is reported.

A review of the medical literature since 1916 indicates that this represents the first reported case.

REFERENCES

1. Haubrich, R.: Mitteilung eines Falles von Herzwaneurysma nach akuter Bleivergiftung, Klin. Wchnschr. **24-25:**754-756, 1947.
2. Beintker, E.: Zu der Arbeit von Richard Haubrich: Mitteilung eines Falles von Herzwandaneurysma nach akuter Bleivergiftung, Klin. Wchnschr. **26:**473-474, 1948.
3. Hirschfeld, E.: Angina Pectoris Saturnina, Ztschr. f. klin. Med. **104:**698-712, 1926.
4. Stoll, M.: Ratio medendi. Uebers. G. L. Fabri. Breslau u.a.O. 1798, II, 1; Wein, Beytrage 1, 1. 1781.
5. Andral, G.: Medizinsche Klinik, II. Bd. 2. Teil. Übersetzt von H. E. Flies. Quedlinburg und Leipzig, 1843.

Book Review

ELEKTROKARDIOGRAPHIE FUR DIE ARZTLICHE PRAXIS, Prof. Dr. Erich Boden, ed. 7, Darmstadt, 1952, Dr. Dietrich Steinkopff, 287 pages, 246 figures, Price D. M. 26.

The first edition appeared in 1932 and was followed by five more in the short interval of six years thus making this the electrocardiographic textbook with the largest number of editions. The seventh edition has been, for the greater part, rewritten and most of the illustrative material is new.

The book is written for the practitioner, and the material is presented in the form of twenty-one lectures. The author has been active in electrocardiographic research and teaching for forty years, and his great teaching experience is reflected in the simplicity of presentation and the large number of excellent diagrams and illustrations.

The book is divided into two parts: the theoretical and experimental basis (Lectures 1 to 9), and the practical application (Lectures 10 to 21). It is primarily based on German information; there is hardly any reference to the postwar American electrocardiographic literature. For the American reader, the condensed presentation of current German theory and interpretation is of interest.

The electrocardiogram is interpreted on the basis of spatial vectorcardiography but limited mainly to mean vectors. The interpretation on the basis of local patterns ("Unipolar Electrocardiography") is rejected, and in this the author is in agreement with an increasing number of American electrocardiographers. Thus, the book has a certain parallel in Grant and Estes' "Spatial Electrocardiography" but includes also other aspects of electrocardiography. In the analysis of spatial vectors the author refers mainly to Gillmann's work.

It is consistent with this approach that all electrocardiograms used for illustrations are taken with a three-channel apparatus, and this is also an advantage for the analysis of extrasystoles and other types of arrhythmias. On the other hand, it is surprising that no illustrations of electronically recorded spatial loops are given.

The author's experiments on the isolated dog's heart, beating in a bath with Tyrode's solution, are reported in some detail. This is an excellent preparation for the demonstration of positional effects versus lesions. The importance of the angle between the mean QRS and T vectors, which remains the same in positional changes but may be altered in lesions, is stressed. A negative T_3 is considered as normal in left QRS axis shift (the angle between QRS and T being normal), but abnormal in right QRS axis shift (the angle between QRS and T being enlarged).

The important problem of normal standards is not adequately treated, and most of the normal standards given are much too conservative, which will result in false diagnoses of abnormality in healthy people. It is suggested that ". . . by frequent inspection of ECG's you will obtain very soon an estimate for the correct amplitude relationships of the various deflections." This reliance on a subjective estimate, instead of valid standards, invites misinterpretation. It is of interest that a large Q_3 is, as a rule, considered as a normal peculiarity of the vector, although it is admitted that occasionally it may represent a posterior wall infarct residuum. In this country the opposite tendency prevails.

The section entitled "Practical Application" is presented in the form of individual cases, with a short history and summary of other clinical findings. With this the author exceeds the scope of an electrocardiographic textbook; he discusses clinical aspects of the various lesions including prognosis and the therapy of arrhythmias. There is more to be said against such extension than for it. The data are too fragmentary to give a proper evaluation of the individual patient, and overemphasize the importance of electrocardiography. In arrhythmias there is no definite correlation between disease and electrocardiogram, and for this reason individual case presentations

are irrelevant and potentially misleading. In infarct, or right or left ventricular hypertrophy, a correlation to autopsy findings would have been more pertinent than the clinical picture which is fairly typical for the cases selected.

In certain points one can disagree with the interpretation, for instance, arborization block (with normal P-R interval) is presented as evidence for bilateral bundle branch block. No differentiation between bundle branch block and ventricular conduction defects is made. Septum involvement in myocardial infarct is diagnosed only if the infarcted area is so large that it involves the precordial leads as well as Leads I and III. The discussion of pulmonary infarct is also inadequate.

It should be kept in mind, however, that the book is written for the practitioner, and, as such, represents a very readable introduction to the fundamentals of electrocardiography. The absence of any bibliography is regrettable, especially for the American reader.

E. S.